

What can Scalar Coupling Constants tell us about the Conformation of the Glycosidic Linkage?

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Introduction

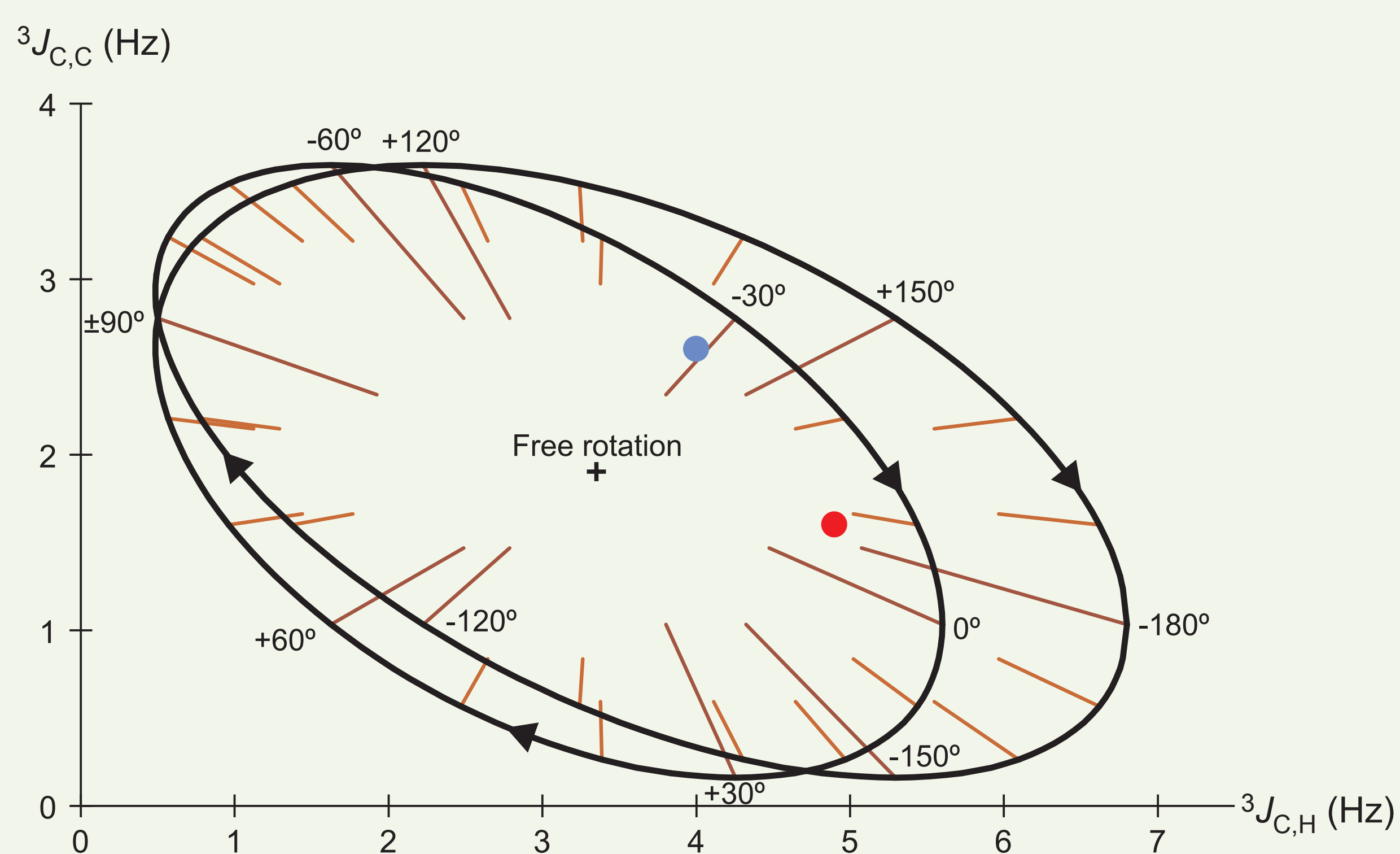
Conformational analysis of biomolecules in solution has traditionally relied on the measurement of nuclear Overhauser effects (NOE). Whilst short ^1H - ^1H inter-residue distances that give rise to NOE are abundant in proteins they are scarce in carbohydrates. The interpretation of NOE derived distances is further complicated by the flexibility exhibited by many carbohydrates.

Scalar coupling constants (J -values) are often easier to interpret since they are related to torsion angles via Karplus-type relations. In oligosaccharides there are two types of 3J -values that are related to the glycosidic torsions φ_{H} and ψ_{H} ; $^3J_{\text{C,H}^1}$ and $^3J_{\text{C,C}^2}$. Measurement of $^3J_{\text{C,C}^2}$ requires ^{13}C -labelled compounds to achieve sufficient sensitivity.

Figure 1: $^3J_{\text{C,C}}$ versus $^3J_{\text{C,H}}$.

The experimental values from $\beta\text{DGalp}(1\rightarrow3)\beta\text{DGalpOMe}$ ($^3J_{\text{C1',C2}}=2,6$; $^3J_{\text{C1',H3}}=4,0$)³ and $\beta\text{DGalp}(1\rightarrow4)\beta\text{DGlcOMe}$ ($^3J_{\text{C1',C5}}=1,6$; $^3J_{\text{C1',H4}}=4,9$)⁴ are indicated in blue and red respectively.

(The corresponding ψ_{H} torsion angles are indicated with numbers and ticks)



Possible combinations of coupling constants

From a plot of theoretical $^3J_{\text{C,C}}$ versus $^3J_{\text{C,H}}$ (fig. 1) for all torsion angles it is possible to draw several conclusions.

* There are several regions where it is impossible to differentiate between conformations that differ by $\sim 180^\circ$.

* In a few favourable cases it is possible to find unique solutions.

There is an additional coupling constant available for ψ_{H} but this does not affect the general conclusions.

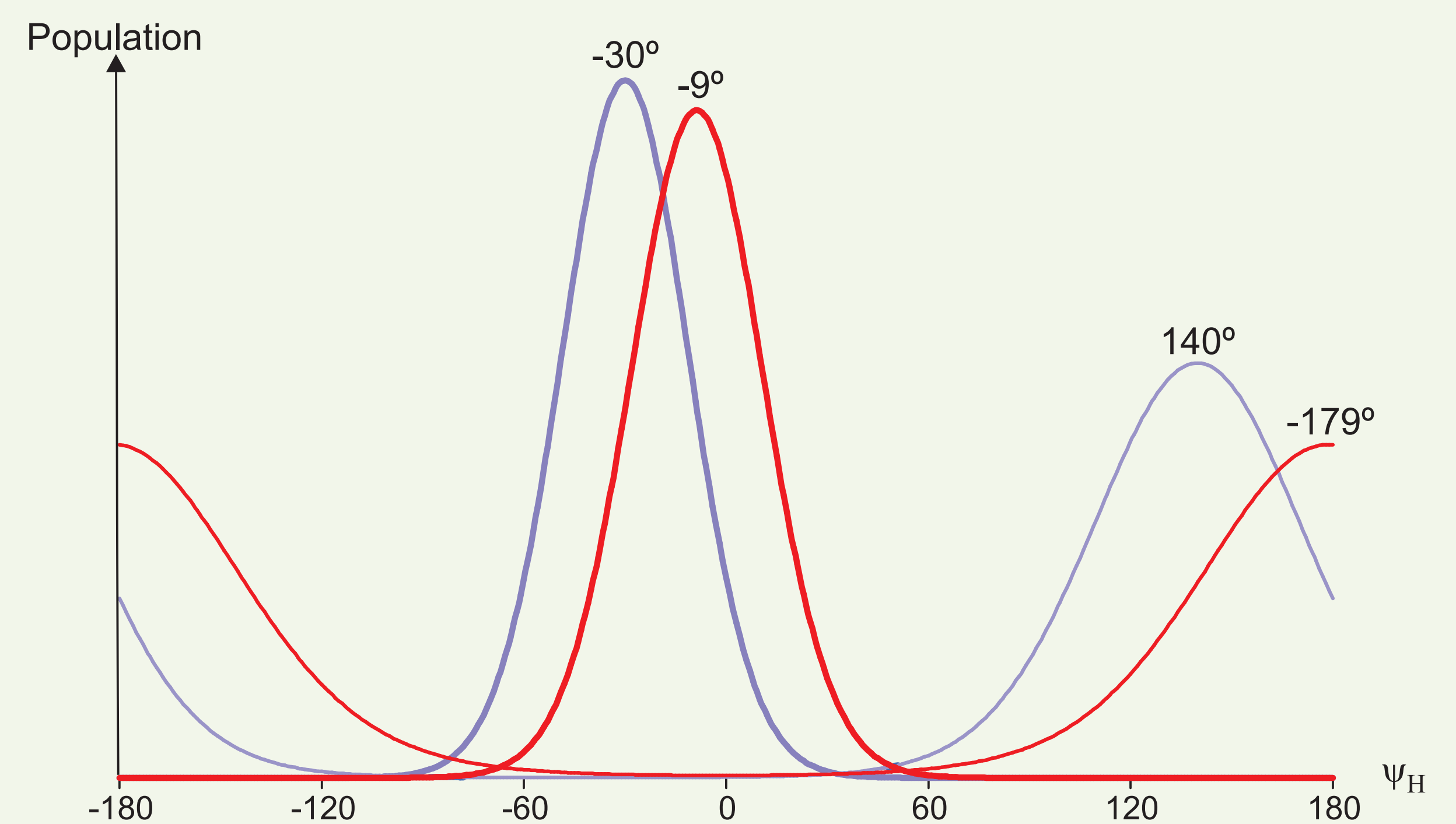
Determining the glycosidic torsion angles

If it is assumed that a glycosidic linkage is relatively rigid it is possible to determine the φ_{H} or ψ_{H} torsion angle from a plot of the root-mean-deviation between the theoretical and experimental coupling constants. By this simple method all possible solutions are found. It is also easy to add other constraints. Two such plots are shown in figure 2.

The flexibility of glycosidic torsion angles

Gaussian distributions that minimise the difference between theoretical and experimental 3J -values (figure 3) can be calculated. Not only is it then possible to obtain the glycosidic torsion angles but their flexibility can also be estimated. The preferred torsion angle obtained by this method is similar to that from the simpler root-mean-square treatment. However since there are two degrees of freedom in the Gaussian functions additional data are required to verify the accuracy of the results.

Figure 3: Population density calculated from coupling constants as function of the ψ_{H} torsion angle for $\beta\text{DGalp}(1\rightarrow3)\beta\text{DGalpOMe}$ (blue) and $\beta\text{DGalp}(1\rightarrow4)\beta\text{DGlcOMe}$ (red). Thin lines correspond to alternate solutions.



Conclusions

Using coupling constants new information about the flexibility and conformational preferences of glycosidic linkages can be obtained. There are however several limitations inherent in this approach which have to be remembered. Most difficulties can be avoided by including additional experimental restraints, e.g. NOE.

We are now preparing several ^{13}C -labelled disaccharides in which $^3J_{\text{C,H}}$ and $^3J_{\text{C,C}}$ values will be measured to determine their structure and flexibility.

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Figure 2: Root-mean-square deviation between calculated and experimental 3J values as function of ψ_{H} torsion angles in $\beta\text{DGalp}(1\rightarrow3)\beta\text{DGalpOMe}$ (blue) and $\beta\text{DGalp}(1\rightarrow4)\beta\text{DGlcOMe}$ (red).

