# Calculation of Raman Optical Activity spectra of monosaccharides : how to handle hydration effects?

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**Résumé**

Despite their involvment in a wide range of biological processes, understanding of carbohydrates' key structure-function relationships, responsible for their activity, is still extremely limited. Indeed, mainstay structural analysis techniques (X-Ray, NMR) are usually not applicable to complex carbohydrates. However, Raman spectroscopy provides the required sensitivity to extensively characterise their molecular structure and interactions.
We report calculations of the Raman and Raman optical activity (ROA) spectra for the two monomeric building blocks glucuronic acid (GlcA) and N-acetyl-glucosamine (GlcNAc) utilizing density functional theory combined with molecular dynamics (MD) simulations to provide an explicit hydration environment. We achieve a significant improvement in accuracy over the more commonly used gas phase and polarizable continuum model (PCM) approaches, resulting in an excellent level of agreement with the experimental spectrum.

Modeling the ROA spectra of carbohydrates has until now proven a notoriously difficult challenge due to their sensitivity to the effects of hydration on the molecular vibrations involving each of the chiral centers. The details of the ROA spectrum of methyl-$\beta$-D-glucose are found to be highly sensitive to solvation effects, and these are correctly predicted including those originating from the highly sensitive low frequency vibrational modes. This work shows that a thorough consideration of the role of water is pivotal for understanding the vibrational structure of carbohydrates and presents a new and powerful tool for characterizing carbohydrate structure and conformational dynamics in solution.
The outcome of this work opens on further investigations, as the identification of spectra-structure relationships for key carbohydrate subunits, and the development of MD force-fields for the accurate MD simulation of carbohydrates in solution.

**Mots-Clés:** Carbohydrate, Raman spectroscopy, ROA, QM/MM, DFT, hydration effect, explicit solvation, MD

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