Stereofitter: new multiparameter 3d structure elucidator

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The ability to elucidate a *de novo* natural product structures in an automated manner has been considered a holy grail in chemistry for many years. [1] Over the last decades, NMR spectroscopy has experienced enormous advances, both in methodology (e.g. new pulse sequences, new alignment media, etc) and hardware (higher magnetic fields, cryoprobes, improved sensitivity). In parallel, sophisticated software packages have been developed aimed at automating the elucidation of small molecules from NMR data, although most of them have been focused on the determination of the molecular 2D structural constitution (2D structure).

In this work, we present our latest efforts towards a fully integrated Computer Assisted 3D Structure Elucidation (CASE-3D) system for the elucidation of relative configuration and preferred conformations of small molecules. It has been designed to cover all required tools for the complete 3D elucidation problem. The main elements of this new software package are:

- A 2D structure elucidation from MS and NMR data.
- Automatic enumeration of diastereisomers from a 2D structure constitution.
- Generation of minimum energy 3D conformations for each 2D diastereoisomer.
- Manual and automatic assignments of 2D molecules
- Fully automatic NOESY/ROESY analysis and distance restraints calculations
- ^{1}H and ^{13}C chemical shift predictions using DFT
- NMR parameters fitting using:
  - ^{3}J scalar couplings
  - NOEs
  - Residual Dipolar Couplings (RDCs)
  - Isotropic chemical shifts
  - Residual Chemical Shifts Anisotropies (RCSAs)
- Statistical analysis of the results for stereo-isomers ranking as well as 3D conformational distributions.

The overall architecture of the application as well as illustrative examples will be shown in this work.

[1] Armando Navarro-Vázquez, Roberto R. Gil, and Kirill Blinov, ”Computer-Assisted 3D Structure Elucidation (CASE-3D) of Natural Products Combining Isotropic and Anisotropic NMR Parameters”, *J. Nat. Prod.*, Article ASAP