

Computational Methods in *iSpartan*

Traditional modeling programs offer an assortment of computational methods to the user. Because the time required for a computation is inversely related to the number of approximations used in the computation, it has always seemed reasonable to let the user locate, usually through trial-and-error "experiments", a suitably rewarding balance between computational effort and approximation. The obvious "upside" is unfettered access to a wide range of methods. The "downside" is the burden of actually having to carry out the "experiments".

iSpartan addresses these same issues, time and approximation, from a different perspective. Rather than provide the user with a large number of computational options that can only be explored through time-consuming experimentation, *iSpartan* aims to provide models of meaningful accuracy in the shortest time possible. To do this, only three computational methods are provided: molecular mechanics (MM) based on the Merck Molecular Force Field (MMFF)¹, quantum mechanics (QM) based on density functional theory (DFT) using the EDF2² functional and the 6-31d (6-31G*) basis set, and QM based on the T1³ thermochemical recipe for heat of formation calculations. Furthermore, as described below, *iSpartan* calls upon each method for a particular type of computation. There are no menus in which a user might select between methods.

- Conversion of 2D sketch into 3D model MM
- Conformer searching and ranking MM
- Basic server calculations: geometry, electronics, energy DFT (QM)
- Optional server calculation: IR* DFT (QM)
- Optional server calculation: NMR* DFT (QM)
- Optional server calculation: heat of formation T1 (QM)**
- Models retrieved from database DFT (QM) with T1 (QM) heats of formation

*The DFT results for IR and NMR peak positions are scaled using empirical schemes that have been developed for standard groups of test molecules. *iSpartan* reports the scaled peak positions, not the original DFT values. IR intensities are directly calculated. NMR intensities are assumed to be proportional to the number of identical atoms. Vicinal (three-bond) HH coupling constants (³J_{HH}) are obtained from empirical relationships based on geometry and bond orders.

**All other properties (geometry, charges, etc.) of a model that has been subjected to a heat of formation calculation are derived from the DFT method. The T1 recipe is used solely to generate the heat of formation.

The philosophy underlying *iSpartan's* approach to computation reflects what we believe are the real-world needs of chemists and students, namely, the solving of a chemical

problem. Problems are solved with the help of useful information, but only when that information can be obtained easily and in a timely manner. Information that cannot be easily obtained might as well not exist. Therefore, the goal of *iSpartan* is to make high-quality information (and high-quality models are the richest source of information chemists can access) easily available.

To accomplish this, *iSpartan* makes it extraordinarily easy to draw a 2D structure, convert it into a 3D model, download a previously calculated result of meaningful quality, and extract information from this model. If an entry does not exist in the database, *iSpartan* offers the option of calculating the model's properties (optimized geometry, total energy, electron density distribution, and optional properties) on a computer acting as a server. This is more practical than performing the calculation on the iPad, partly because the server will offer considerably more computing power, but also because this frees the iPad for other uses. The same computation method is used to create models in the database and to perform calculations on the server. This not only saves time and encourages users to stay focused on problem solving, it also guarantees that all *iSpartan* models (and, more importantly, all of the information derived from these models) reflect a consistent set of approximations. Therefore, even when approximations may bias a model, comparisons between models will often be valid because both models will reflect the same bias.

References

- 1) Journal of Computational Chemistry 1996. 17 (5-6): 490–519.
- 2) Australian Journal of Chemistry 2004. 57 (4): 365–370.
- 3) Journal of Physical Chemistry A 2009. 113 (10): 2165–2175.

Estimating Times for Server Calculations.

The time required for calculating the equilibrium geometry and wave function (the latter providing access to the molecular orbitals and the electrostatic potential map) depends on several factors in addition to the size of the molecule. These include the number of independent bond lengths and angles, the "floppiness" of the molecule and the "quality"

of the geometry guess. The table below lists "typical" relative times for this step for six molecules of increasing size.

formula	molecular weight	relative time
$C_4H_{11}NO$	89	1
$C_{11}H_{18}O$	166	10
$C_{14}H_{22}N_2O_2$	250	25
$C_{16}H_{25}N_3O_3$	307	50
$C_{21}H_{37}N_3O_4$	396	100
$C_{24}H_{41}N_3O_6$	468	150

NMR and IR spectra may also be requested as can a heat of formation. Adding an NMR spectrum increases the time by only about 3% while adding an IR spectrum increases it by about 80% (don't ask for it if you don't need to). Finally, adding a heat of formation increases the calculation time by about 20%. Practical considerations (both time and memory) limit calculations to molecules with molecular weights on the order of 600-700 for geometry, wave function and NMR calculations, and 400-500 for IR and heat of formation calculations. NMR calculations are limited to molecules containing elements that are no heavier than Br, and heat of formation calculations to molecules containing only the elements H, C, N, O, F, Si, P, S, Cl and Br.