

# Chiral Spectroscopy: Towards a Reliable Comparison Between Theory and Experiment

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Chiral enantiomers — pairs of dissymmetric molecules that are merely mirror images of one another — often exhibit dramatically different chemical behavior when reacting in chiral environments, and the need to distinguish between such enantiomers drives much of the multibillion-dollar research efforts of the pharmaceutical industry. Enantiomeric pairs also exhibit mirror-image responses to circularly polarized electromagnetic fields in absorption (dichroism), refraction (birefringence), and scattering: if the left-hand enantiomer of a chiral compound preferentially absorbs right-circularly-polarized light, the right-hand enantiomer will preferentially absorb the left-handed light, and vice versa. However, such responses are useful for the identification of the handedness of a chiral sample only if a reliable reference is available. This lecture will focus on our recent work to establish high-level quantum chemical methods such as coupled cluster theory as just such a reference.[1, 2] In particular, we will discuss the impact of various physical factors — electron correlation, basis-set completeness, gauge invariance, molecular vibrations, and solvent — on the predictive capabilities of the coupled cluster model in comparison to both gas- and solution-phase measurements of optical rotation, electronic circular dichroism, and vibrational Raman optical activity. In addition, we will discuss approaches for reducing the computational scaling of coupled cluster methods in order to extend their range of applicability to large chiral molecules and explicit solvent configurations.[3]

[1] T.D. Crawford, “High-Accuracy Quantum Chemistry and Chiroptical Properties,” in Comprehensive Chiroptical Spectroscopy, Vol. 1, N. Berova, K. Nakanishi, R. Woody, and P. Polavarapu, eds., Wiley and Sons, 2011

[2] T.D. Crawford and P.J. Stephens, “A Comparison of Time-Dependent Density-Functional Theory and Coupled Cluster Theory for the Calculation of the Optical Rotations of Chiral Molecules,” *J. Phys. Chem. A* **112**, 1339-1345 (2008).

[3] T.D. Crawford, “Reduced-Scaling Coupled-Cluster Theory for Response Properties of Large Molecules,” in Recent Progress in Coupled Cluster Methods: Theory and Applications, P. Carsky, J. Pittner, and J. Paldus, eds., Springer, pp. 37-55, 2010.