PREDICTION OF MOLECULAR STRUCTURES FROM ROTATIONAL CONSTANTS: A PROPOSAL FOR SOLVING THE INVERSE PROBLEM

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As made clear by E. Bright Wilson's prescient thesis published in Science in 1968,[a] applicability to analytical chemistry has long been a goal for microwave spectroscopy. This comes as no surprise, as the high-resolution nature of microwave spectroscopy leads to unparalleled sensitivity to the structures of molecular analytes. However, in the absence of isotopologues, determination of an unknown molecule's identity can be difficult by the experimental rotational constants alone. Although a structure maps trivially into its rotational constants, the reverse is not necessarily true as some structural information is lost. Yet, one can imagine a trained machine that outputs likely molecular structures by intelligent interpretation of the observed rotational spectroscopy. This is the inverse problem for rotational spectroscopy – instead of predicting constants from structures, the goal is to predict structures from constants.

Recent developments in machine learning have led to success in decoding multidimensional chemical parameter spaces from massive, enumerated libraries of molecular structures.[b] In order to apply such methods to the inverse problem, there are critical questions that are still unanswered. For instance, is the mapping of spectrum to molecule single-valued within the uncertainty of calculated rotational constants? If not, what is the average number of reasonable molecules consistent for a random but valid set of rotational constants? Or, is there an efficient and convergent "similarity" metric that compares a target spectrum to a chemical search space, key for developing a molecular "search engine"? With these questions in mind, this talk will present an exploration of, and a proposal for, a potential solution to the inverse problem.

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[a] Wilson, E. B., Science **1968**, *162*, 3849.

[b] [1] Zhou, Z.; Kearnes, S.; Li, L.; Zare, R. N.; Riley, P., *Sci. Rep.* **2019**, *9*, 10752. [2] Gómez-Bombarelli, R.; Wei, J. N.; Duvenaud, D.; *et al.*, *ACS Cent. Sci.* **2018**, *4*, 268.