Learning Multireference Chemistry: Accurate Models for Excited States and Dynamics

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Multireference electronic structure methods are essential for describing chemistry in which a single electronic configuration is not enough: bond breaking, transition-metal reactivity, and excited-state processes are prominent examples. Yet their routine use in complex chemical environments remains limited by computational cost, by the need for robust active-space choices, and by the difficulty of following electronic structure consistently along reaction pathways.

I will discuss recent progress from our group toward making multireference methods more practical, systematic, and transferable. The first example concerns methane C–H activation at metal–oxo sites in metal–organic framework nodes. We have introduced an automated multireference workflow in which the active space is localized on the chemically relevant fragment. This strategy provides a route to applying multireference methods to realistic catalytic environments and to analyzing, across different metal centers, how metal–oxygen bonding, radical character, and electronic structure control reactivity.[1]

The same need for consistency also arises when multireference data are used to train machine learning models. To address this challenge, we developed machine learning potentials trained on multireference electronic structure data together with the weighted active space protocol, which maintains consistent active-space assignments across diverse nuclear geometries. Combined with active learning and enhanced sampling, this approach enables data-efficient molecular dynamics with multireference accuracy. We applied it to TiC^+-catalyzed methane C–H activation, a reaction for which conventional density functional theory struggles because of strong multiconfigurational character.[2]

[1] J. Wardzala, Y. Kim, R. Khurana, M. Mandal, M. Delferro, C. Liu, L Gagliardi From Oxo to Oxyl to Biradical: Systematic Multireference Calculations of Methane Activation at MOF Nodes, *J. Am. Chem. Soc.* **2026**, 148, 27411–27420. DOI: https://doi.org/10.1021/jacs.6c05408
[2] A. Seal, S. Perego, M. R. Hennefarth, U. Raucci, L. Bonati, A. L. Ferguson, M. Parrinello, and L. Gagliardi, Weighted Active Space Protocol for Multireference Machine-Learned Potentials, *PNAS*, **2025**, 122, e2513693122. DOI: 10.1073/pnas.2513693122