Predicting Reaction Selectivity

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Predicting Reaction Selectivity

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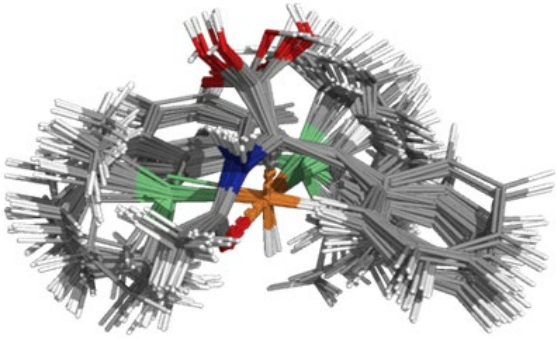
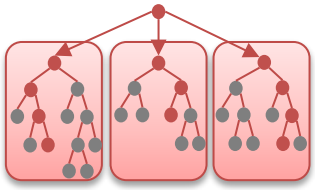
Detailed knowledge of reaction mechanisms will allow prediction of the reaction selectivity, usually by DFT methods. However, such methods are too slow to allow a full exploration of all possible reaction paths for conformationally complex molecules. We explore more efficient and more accurate methods, based on rapid molecular mechanics methods tuned to work for transition states. Our in-house method Q2MM [1] allows prediction of stereoselectivity by screening thousands of transition states for each reaction, as illustrated to the right for asymmetric hydrogenation. More recent examples will be covered in the talk.

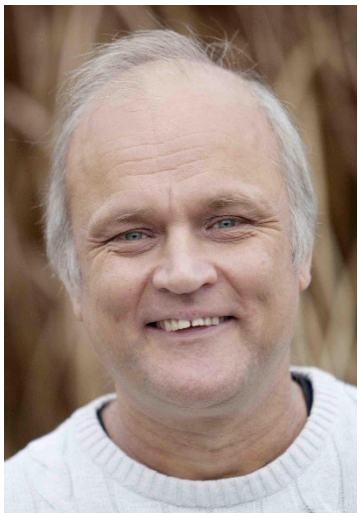




For regioselectivity predictions, where classical force fields are invalid, we instead explore different ways of combining quantum chemical calculations with limited experimental data in machine learning approaches to derive selectivity models [2]. A range of such approaches will be illustrated.

References

[1] E. Hansen, E. Limé, P.-O. Norrby, O. Wiest *Acc. Chem. Res.* **2016**, *49*, 996-1005.
[2] K Jorner, A. Tomberg, C. Bauer, C. Sköld, P.-O. Norrby, *Nat. Rev. Chem.* **2021**, *5,* 240-255.



Per-Ola Norrby was born in Sweden in 1962. He obtained his PhD in Organic Chemistry from KTH, Stockholm in 1992, under the supervision of Björn Åkermark. He then did a postdoc with Barry Sharpless at Scripps in San Diego. A second postdoc with Tommy Liljerfors at DFH in Copenhagen led to an academic career in Denmark, first at DFH, then at DTU, where he became Associate Professor in Organic Chemistry. He moved back to Sweden in 2006 to become a Professor in Organic Synthesis at Gothenburg University. In 2014, he moved to AstraZeneca Gothenburg where he took up a position as Principal Scientist. In 2024, he was promoted to Senior Principal Scientist in Data Science & Modelling, Pharmaceutical Sciences.

Throughout his career, his research interests has focused on reaction mechanism, which have been studied using a combination of experimental techniques and molecular modelling, frequently in collaboration with other research groups. A major focus has been to develop predictive models for stereoselectivity, and to apply these in virtual screening of asymmetric catalysts. In the last decades, he has focused on all aspects of chemical reactivity in the pharmaceutical industry, from synthetic route design to understanding stability and degradation of pharmaceutical products.

He has published >200 peer reviewed articles together with >400 co-authors, and has h-index 68 (Google Scholar). He is a Fellow of Chemistry Europe and of the Royal Society of Chemistry, and a life-time member of the Swedish Chemical Society. In 2019, he received the Ulla and Stig Holmquist Prize in Organic Chemistry from Uppsala university.

Publication lists:

Google Scholar

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Scopus