


Presented by Matt Segall at 12th International ISSX Meeting 2019, Oregon, USA

Presentation Overview

- **Approaches to predicting metabolism** – Empirical vs mechanistic
- **Predicting P450 metabolism** – P450 regioselectivity – Which P450
- **Beyond P450s** – Flavin containing monooxygenases (FMO) – UDP glucuronosyltransferases (UGT)
- **Conclusions**

Quantum Mechanical Models for CYP Reactivity

- Semi-empirical QM methods (AM1) are used for practical calculations
 - Surrogate radical used instead of haem
 - Bridged relationships used to estimate activation energies
 - Corrections applied based on ab initio QM
- Full substrate included in simulation
 - Not 'pattern matching' sites to precalculated energies
 - Includes subtle longer range effects
 - Important when developing a lead series



Hydrogen radical

Thornik et al. (2007), Chem. Inf. Model. 20(1) pp. 210-220

You can download the presentation slides as a [PDF](#)