Artificial force induced reaction method: A computational approach for exploring chemical reactions based on quantum chemical calculations

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ABSTRACT

The motion of atoms during a chemical reaction, called reaction path hereafter, can in principle be elucidated by repeatedly performing quantum chemical calculations at all energetically feasible atomic configurations. However, the number of possible arrangements involved in a reaction path can be huge. Previous studies have thus relied on assumptions, i.e., human inputs, concerning the atomic configurations along the targeted reaction path.

The human inputs may bias the results. To avoid that, we have developed an automated reaction path search method called artificial force induced reaction (AFIR) [1]. AFIR explores possible reaction paths automatically by inducing geometrical transformations in a molecule systematically using a virtual force. Combining it with a chemical kinetics method called rate constant matrix contraction (RCMC), on-the-fly kinetics simulation can be performed (FIG. 1).

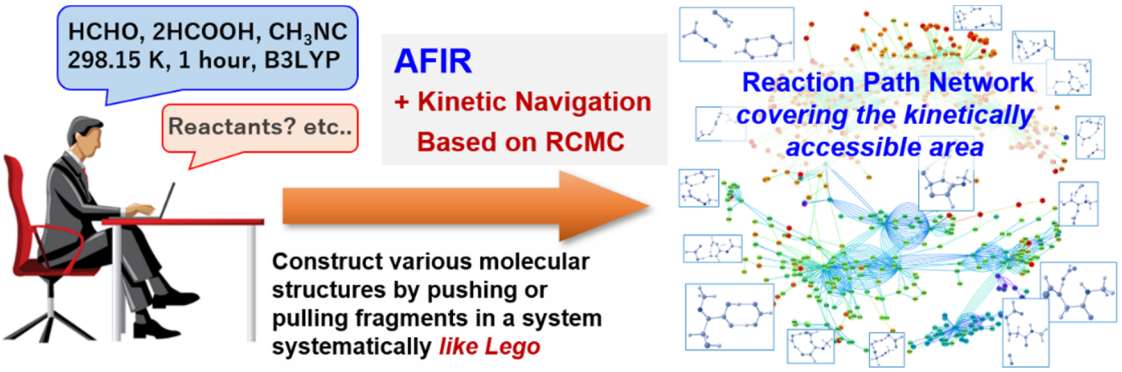

FIG 1. A schematic illustrating on-the-fly kinetics simulation by AFIR and RCMC. Based on the input, i.e., reactants, reaction temperature, reaction time, and computational level, AFIR finds many reaction paths. RCMC identifies the most feasible reaction path from the resultant network.

Recently, we proposed a concept, quantum chemistry-aided retrosynthetic analysis (QCaRA). QCaRA predicts reaction paths affording a given product by an inverse reaction path search from the product toward various reactant candidates using AFIR. In a proof-of-concept study, we set difluoroglycine as the synthetic target. Then, a new synthetic route of producing a difluoroglycine derivative was proposed as the reverse process of one of the obtained reaction paths [2]. Further generalization of the algorithm to perform QCaRA to predict multistep reactions [3] and a new design strategy of transition metal catalysis [4] will also be presented.

REF.
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4. Matsuoka, W.; Harabuchi, Y.; Maeda, S. *Submitted* (Preprint is available in *ChemRxiv*).