Computational Planning of Synthesis of Natural Products

INQUIRY

In order to model and understand molecular phenomena, a variety of computational chemistry approaches have been applied in the synthesis of natural products. Computational analysis is able to help chemists achieve concise total syntheses of various natural products. With the development of algorithms, it is possible to effectively identify the chemical bond break and realize the design of unprecedented synthetic routes through quantum chemical calculations. In planning the syntheses procedure, chemists take a cue from how nature builds the molecules, identifying and focusing on the key biosynthetic step. Alfa Chemistry uses computational techniques to generate new insights into the interactions of fundamental chemical forces in the field of complex small molecule synthesis. We have introduced multiple computational techniques to plan the synthesis procedure of natural products.

Application of Computational Tools in Planning of Synthesis of Natural Products

- Rationalize the reaction outcomes
- Predict the performance of a new system
- Guide the synthetic design

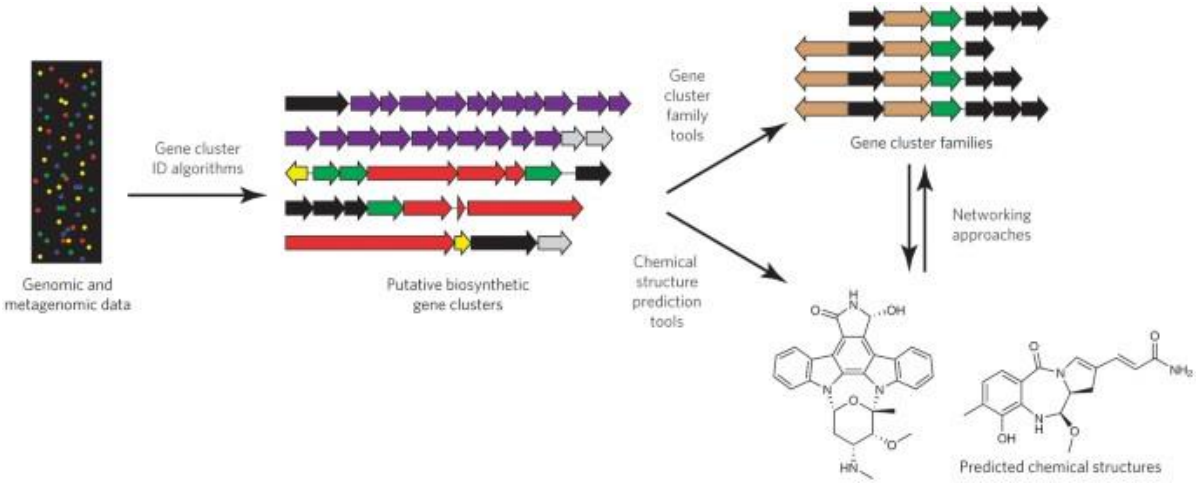

Figure 1. Computational approaches to natural product discovery. (Medema, M. H.; Fischbach, M. A. 2015)

Our Synthetic Route

At Alfa Chemistry, we use our rich knowledge of computation chemistry to identify possible bond-making steps in a synthesis and rationalize why a synthesis work after completion. Our team take the less explored strategy of using computation to evaluate variations on a single synthetic step. Here is our planning process:

- We firstly identify possible precursors that could access the key biosynthetic step.
- Then, computational methods are used to model the energy of reactions with each precursor to evaluate which one has the highest likelihood of success.
- Our experts design a synthetic route that proceed through that intermediate.

Our Services

At Alfa Chemistry, we support various theoretical methods for natural product synthesis research:

- Quantum mechanics (QM)

We provide molecular orbital (MO) calculation methods based on the Schrödinger equation and density functional theory (DFT) calculations based

on the Kohn-Sham equation. The QM method is mainly used to evaluate the reactivity or properties of small molecules. The general steps are:

1) First, we perform a transition state (TS) search.

2) Then, a frequency calculation is carried out to ensure that TS has only one imaginary frequency.

3) Finally, we conduct an intrinsic reaction coordinate (IRC) calculation to obtain the reactants and products. The commonly used theoretical methods are mPW1PW91/6-31+G (d,p), B3LYP/6-31+G(d,p), *etc*.

In addition, in order to reduce the amount of calculation, we often use the cluster model method in which only a few residues around the substrate and the active center are considered.

- Molecular dynamics (MD) simulation

  We use the MD simulation method which is developed based on Newton's equation. The calculation cost is low, and it can simulate the structural changes of enzymes over time. In general, we apply this method to reactions that require calculations of free energy with low accuracy, especially reactions that do not need to consider chemical reaction changes.

- Quantum mechanics/Molecular mechanics (QM/MM)

  QM/MM method divides the system into two areas: the catalytic activity center is calculated using the QM method, and the other areas are calculated using MM. Furthermore, the QM/MM MD method can be combined to balance calculation accuracy and cost.

Alfa Chemistry's Advantages

- We are capable of designing complex algorithms to design plausible routes to complex natural products.
- Alfa Chemistry provides knowledge of organic chemistry and data-based artificial intelligence routines to support the computational synthesis planning.

- Our expert-level automated synthetic planning is feasible which is developed based on the continued improvements to the reaction knowledge base and further code optimization.

Our computational planning of synthesis of natural products services remarkably reduce the cost, promote further experiments, and accelerate the process of drug design for customers worldwide. Our personalized and all-around services will satisfy your innovative study demands. If you are interested in our services, please don't hesitate to contact us. We are glad to cooperate with you and witness your success!

Reference

1. Medema, M. H.; Fischbach, M. A. Computational approaches to natural product discovery. *Nature Chemical Biology*. 2015, 11(9): 639.

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https://wavefunction.alfa-chemistry.com/services/computational-planning-of-synthesis-of-natural-products.html