【Grant-in-Aid for Transformative Research Areas（Ｂ）】

Creation of Gigantic Chemical Space Science: Establishment of Scientific Principles for Finding Useful Compounds from Hundreds of Millions of Unknown Compounds

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Research Area Information	Number of Research Area : 23B203　Project Period (FY) : 2023-2025 Keywords : Chemical space, chemical informatics, theoretical chemistry, precise organic synthesis, automated synthesis

Purpose and Background of the Research

●Outline of the Research

Various chemical substances produced by chemical reactions have become indispensable to modern society as pharmaceuticals and functional materials. On the other hand, the chemical substances that mankind has obtained so far are only a small part of the vast combination of elements (huge chemical space), and there are still many unexplored areas. The number of possible compounds is thought to exceed the power of 10 to the 60th power, even when limited to those with molecular weights of 500 or less. Still, the compounds that have been made available to mankind so far (for example, those registered in the National Institutes of Health repository) are on the order of the 9th power, leaving a huge unexplored chemical space. On the other hand, it is challenging to handle such a huge chemical space directly using conventional synthetic organic chemistry methods, and a new scientific theory is required to find useful compounds that lie in this huge unexplored chemical space.

This proposal aims to create and apply "Gigantic Chemical Space Science," which integrates theoretical chemistry, information science, organic synthetic chemistry, and automated synthetic robot technology, and to establish a new scientific principle to efficiently search for useful compounds in the gigantic chemical spaces containing several hundred million unknown compounds. To establish the scientific principle, four groups (Information Science, Theoretical Chemistry, Experimental Chemistry, and Robotics) are organized, and each group sets its own research goal to achieve the goal and promotes research by solving problems through close collaboration among the groups (Figure 1).

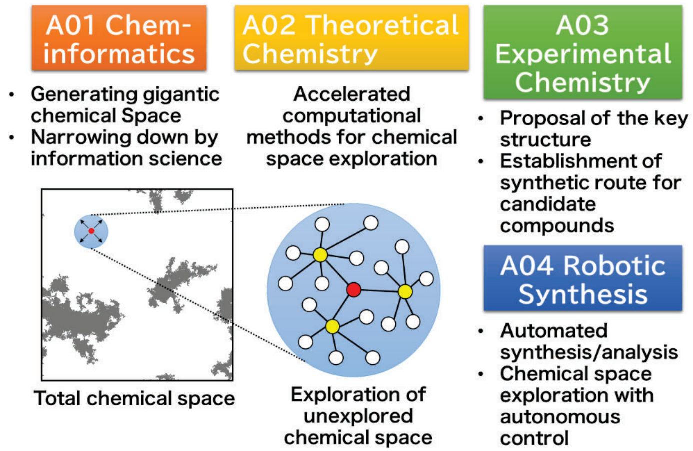

Figure 1 Research plan in our group

●A specific research motifs

As a specific research motif, our group focuses on cyclic oligoquinolines with quinoline rings as the basic framework. Prof. Naoya Kumagai, who heads the Experimental Chemistry Group and is an expert in the development of new reactions and materials, has succeeded in developing a novel molecular motif, triquinoline, consisting of three quinoline skeletons connected in a ring shape, and reported on its photophysical properties (Figure 2). Although triquinoline has an extremely simple structure, its derivatives and analogues are completely unexplored molecules, and are considered to be useful as a stepping stone to unravel the "giant chemical space".

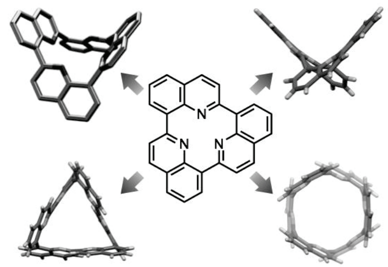

Figure 2 Structure of triquinoline (center) and its derivatives and analogues

Expected Research Achievements

●Establishment of "giant chemical space science"

In order to prove the concept of "giant chemical space science," we plan to search for chemical spaces focusing on photophysical properties, initially using quinoline rings as the basic skeleton, but this can be applied to various academic fields by changing the basic skeleton and target properties (Figure 3). As an example, by setting various heterocyclic skeletons and polycyclic aromatic rings as the basic skeleton and taking hydrophobicity/hydrophilicity and affinity to specific proteins as the physical properties, we believe this concept can be applied to the development of biochemical probe molecules and drug discovery and is expected to expand into a wide range of fields.

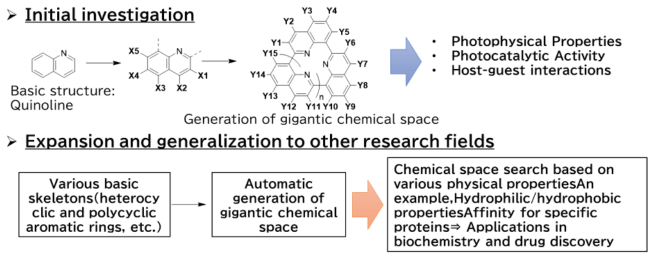

Figure 3 An example of the expansion of "Giant Chemical Space Science" into other research fields

● Promotion of fusion research and establishment of new research fields

In addition, it is possible to quantitatively evaluate the degree of similarity between research fields by reviewing the "chemical space" of compounds that have been used in various research fields and comparing the chemical space in each research field (Figure 9). This can be used to promote fusion research by finding research fields that share a common chemical space, or to establish a new research field that connects similar research fields, and to expect the formation and creation of new fusion research fields.

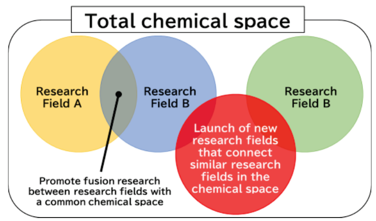

Figure 4 Analyzing research fields from the perspective of chemical space, promoting fusion research, and launching new research fields

Homepage Address, etc.	Website of this research area "Giant Chemical Space“ https://gigantic-chemical.space/