Title of Project： Fusion of Computer Science, Engineering and Mathematics Approaches for Expanding Combinatorial Reconfiguration

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Number of Research Area：20B401　Researcher Number：40431548

【Purpose of the Research Project】

Combinatorial reconfiguration is a novel algorithmic concept that provides mathematical models and analysis for “transformations over state spaces.” Its appearance ranges from theory to applications. However, its technical achievements are hard to access. This research project aims at founding a common infrastructure for utilizing and applying the algorithmic technology of combinatorial reconfiguration. The research groups consist of computer scientists, engineers, and mathematicians who cooperatively work for establishing the algorithmic foundation, the implementation technology foundation, and the mathematical foundation of combinatorial reconfiguration. Then, we establish the fundamental theory that is useful for software development and integration.

【Content of the Research Project】

Consider power distribution systems as a concrete situation of combinatorial reconfiguration. A power distribution network is designed as it has multiple numbers of routes for supplying electricity. For example, the Japan standard model of power distribution networks has approximately ten octodecillion alternatives for the choice of network configurations. Even the computation of a single optimal configuration among them is out of reach. Furthermore, even if we may compute a single optimal configuration, we encounter another issue. Namely, upon a switching procedure to reconfigure the current configuration to the optimal one, we may not allow any power failure during the process. This requires us to develop a switching procedure that does not cause power failure upon the process over the state space consisting of approximately ten octodecillion alternatives from the current configuration to an optimal configuration. This is a typical example of “transformations over state spaces” which is the target of the algorithm theory called “combinatorial reconfiguration.”

Figure 1. Example of power distribution systems

Combinatorial reconfiguration appears in various areas of research and practice, and experiences successes ranging over several fields. However, the technology of combinatorial reconfiguration is only available to the experts who study it, and researchers in other areas and practitioners need to access those experts. On the other hand, Mathematica for symbolic computation and SAT solvers and IP solvers for combinatorial problems provide the foundations for non-experts, who can easily access those technologies and solve problems in their domains. Regretfully, combinatorial reconfiguration lacks such a common infrastructure.

In this research project, computer scientists, engineers, and mathematicians cooperatively work for founding a common infrastructure for utilizing and applying the algorithmic technology of combinatorial reconfiguration.

Group A01 with the computer science background founds “algorithmic meta-theorems” for combinatorial reconfiguration, and aims at automatic generation of combinatorial reconfiguration algorithms.

Group B01 with the engineering background founds the “implementation technology” for combinatorial reconfiguration, and aims at software development as a communication infrastructure common to theoretical research and industrial applications.

Group C01 with the mathematics background founds the “mathematical theory” for combinatorial reconfiguration, and proposes new mathematical methods that are useful for combinatorial reconfiguration.

【Expected Research Achievements and Scientific Significance】

As combinatorial reconfiguration appears in various fields, if the common infrastructure is established, the concept of “computation” can be introduced in a wide range of fields. This research project will provide the way of computation even for non-experts, and an opportunity for these fields to bring about new changes.

【Key Words】

- Combinatorial reconfiguration: A research topic that models transformations over state spaces, and analyzes the complexity of algorithms and computation.

【Term of Project】 FY2020-2022

【Budget Allocation】 123,700 Thousand Yen

【Homepage Address and Other Contact Information】

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Title of Project： Synergy pharmaceutical science: understanding and design of compound combination effects by integrating information, material, and life sciences

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【Purpose of the Research Project】

Chemotherapy that utilizes the synergistic effect of a combination of multiple drugs (drug synergy) has been recognized as an effective method for treatment of multifactorial diseases such as cancer and neurodegenerative diseases. In addition to enhancing the therapeutic effect, it has the advantages of reducing the amount of individual drugs and reducing the frequency of serious side effects. However, since irrational drug combinations lead to harmful side effects, it is necessary to identify the optimal drug combination, which is extremely difficult. To date, many of the drug synergies have been discovered accidentally in clinical studies, and the molecular mechanism of disease-specific drug synergies is not well understood. Drug synergies are involved in the interaction between drugs and biomolecules, but the relationship with drug synergies is unclear.

In recent years, in the fields of material science and life science, various big data on genes, proteins, drugs and compounds (e.g., genome, omics, combinatorial chemistry) have been generated and accumulated. On the other hand, in the field of information science, the development of artificial intelligence (AI) and machine learning technologies is remarkable. In this research, we advocate a new academic field called "synergy pharmaceutical science" that systematically studies drug synergies, and aim at understanding of drug synergistic effects and construction of design methods through the collaboration of information science, material science, and life science.

【Content of the Research Project】

The "synergy pharmaceutical science" advocated by this research will be a new academic area created by connecting the fields of life science and material science through big data analysis by AI in information science. Bioinformatics for AI analysis of biomolecular data, chemoinformatics for AI analysis of drug/compound data, medical data analysis, organic chemical synthesis, and biological experiments will be performed. Our research team consists of three groups: AI group, medical data group, and pharmacology group.

In the group A01 (AI group), we will extend the technology of the machine learning method for predicting the target molecule and new efficacy of the drug to the combination of drugs, and develop new machine learning methods for predicting the combination of drugs and synergistic effects in this study. In addition, we will develop a mathematical model of the combination problem of drugs and biomolecules and its theoretical solution. Furthermore, the chemical structure of compounds with synergistic effects is predicted and designed.

In the group A02 (medical data group), we will analyze medical big data and develop data mining technologies for predicting drug pairs and drug combinations that have a disease-preventing effect.

In the group A03 (pharmacology group), we will construct pathological models for verifying the synergistic effects of the predicted drug synergies, and confirm the predicted pharmacological actions experimentally at the cell level and animal level.

【Expected Research Achievements and Scientific Significance】

To date, drug synergies have been discovered by chance in clinical studies. In this study we use AI to explore all possible combinations of drugs, which could solve the problem of combinatorial explosion.

Drug synergies are analyzed with respect to disease-specific abnormal expression genes and drug-responsive abnormal expression genes. Since drug synergies may be caused by the result of dynamic reactions in biological systems, the use of omics data will lead to accurate understanding of drug synergies.

Drug synergies are actually used in medical treatment in the form of multidrug therapy, but the drug selection criteria depend largely on the experience and knowledge of doctors and on the type of disease and the pathology of the patient. In this study, we can innovate the concept of polypharmacology by establishing a new strategy based on drug synergies supported by scientific evidence.

Many modern diseases such as cancer and dementia are multifactorial diseases, and the therapeutic effect is weak by single drug administration alone. Therefore, multidrug drug therapy is expected to be useful. The number of cancer patients in Japan is 890,000, and the number of dementia patients in Japan has reached about 4.62 million as of 2012. The results of this research can contribute to medical treatment.

【Key Words】

Drug synergy: Synergistic effects of combining multiple drugs

【Term of Project】 FY2020-2022

【Budget Allocation】 119,700 Thousand Yen

【Homepage Address and Other Contact Information】

http://labo.bio.kyutech.ac.jp/~yamani/synergy/