[Special feature]

Artificial Intelligence

From personal to societal knowledge

Computers replace human beings in leading to answers.
NII is carrying out extensive informatics-based artificial intelligence (AI) research.
The culmination of this research will be the fusion of AI and a variety of sciences, and the further evolution of Web services.
AI research now attracts considerable attention as a methodology for pursuing the "knowledge" that is vital to creating a prosperous society.

NII Interview

Working to Unravel the Secrets of Biological Activity Through Inference

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Artificial intelligence establishes hypotheses, tests them, and confirms them

Yoshida The image computers that one may have is one of being good at performing calculations in accordance with defined rules, but being unable to handle things which do not follow rigidly pre-determined lines. Professor Inoue, you're researching mechanisms which transcend that conventional wisdom — in other words, systems where computers infer, in the form of hypotheses, the rules necessary to reach a conclusion. That approach is currently being used in the field of systems biology. Could you start by telling us what it means to discover a hypothesis through inference?

Inoue A famous example of syllogism is: A "All men are mortal ", B "Socrates is a man", C "Socrates is also mortal". A is the major premise or rule, B is the minor premise, and C is the conclusion. Given general principle A, and individual fact B, syllogistic logic leads to conclusion C, which is mathematically correct. This is called deduction. If one only has A "All men are mortal", and C "Socrates is mortal", what sort of premise could be added to make this conclusion true?

Yoshida The minor premise that "Socrates is a man"?

Inoue Yes. One can infer the hypothesis that "Socrates is a man", and confirm whether or not that is correct. This is called abduction(*1). Conversely, starting with B "Socrates is a man", and C "Socrates is mortal", and discovering major premise A "All men are mortals" is called induction(*2).

Yoshida Discovering something like that seems to me to be the type of creative effort that is the domain of humans. Are you talking about a computer creating this new hypothesis?

Inoue We infer hidden relations and constraints that are logically possible, and in principle those inferred hypotheses can contain newly created theories for human beings.

Yoshida Is this field of inference-based hypothesis finding a new one?

Inoue No, it's been researched in the AI field for over 20 years. What's new about our research is that our method works well even with incomplete knowledge.

Discovered by foreign researchers, and applied to systems biology

Yoshida Professor Inoue, how did you come to be involved in the field of automated reasoning?

Inoue When I was a university student, I majored in algorithms. In order to quickly and efficiently solve problems, we need to consider the types of instructions to be used, how to combine and order them, and what procedures to follow. I was also very interested in game searching. You have to select from a massive range of continuously changing options of what to do in order to achieve your ultimate objective of victory over your opponent, while the opponent is also assumed to take the best strategy. The model for this is human intelligence.

Yoshida So you started in what could best be called the field of mathematical computation applied to intelligent search, but this served as the background to your entry into the world of logical inference

Inoue Indeed, when we consider a dynamic situation in which our knowledge and observations change from time to time, the problem that we need to solve also changes accordingly. In such a case we need to infer about past and future states using a more intelligent methodology. I thus became interested in basic theories of reasoning under incomplete knowledge.

Yoshida When did you start on the path to your current research?

Inoue It was around 2001. The hypothesis finding method that I introduced in 1991 was noticed by a British post-genomic research group, who asked me some questions. They were involved in some ambitious research, using a robot to generate hypotheses regarding gene functions, plan experiments based on those hypotheses, perform the experiments, and produce feedback based on those results, all automatically. They believed that my method could be used as the theoretical background for their hypothesis generation. I later had similar inquiries from French researchers, who I performed joint research with. We began full-fledged application of our "SOLAR(*3)" method. The theme we chose was identifying which enzymatic reactions in metabolic pathways are accelerated and which others are inhibited

Yoshida There are many computer learning and hypothesis finding techniques. What sets SOLAR apart?

Inoue It can produce logically possible hypotheses for a wide range of problem classes. It is especially unique in that it possesses features for filling in missing knowledge or data in the form of hypotheses. In order to do this, computationally efficient methods to generate candidate hypotheses must be developed. When arriving at conclusions from incomplete premises, there are many conceivable candidates which should be filled in. However, checking each one, one by one, would take a tremendous amount of time. In some cases, the number of candidates explodes, and cannot be narrowed down within a practical time. In order to avoid this situation, we incorporate a statistical hypothesis evaluation method so that only top ranked hypotheses are verified in subsequent experiments.

Yoshida Computer technologies such as algorithms and game search concepts are utilized in a comprehensive manner. So this SOLAR system is used in systems biology, but what exactly is systems biology?

Searching for the missing link of biological activity

Inoue Systems biology is concerned with an integrated understanding of the different interrelated elements that make up life activities, which it treats as a single system.

Yoshida Biology has traditionally taken a functional explanation approach, saying that mitochondria are related to cell respiration, or that ribosomes copy DNA and create new proteins.

Inoue Biology has until now focused on separating individual structures and parts, and explaining what they do, and this is still the primary approach used in bio research. The goal of systems biology, on the other hand, is exploring the relationships between these separate components, which are then put back together again into a cohesive whole.

Yoshida It takes different levels of biological components, both large and small—organs, the cells that make them up, nerves, DNA, enzyme, proteins and metabolites—and looks at them as a single system?

Inoue Yes, but gathering everything into a single entity is not immediately feasible. Instead, for, say, a single function, it looks at how its component elements behave, how they interrelate, and what function is produced through those interrelationships. For example, within cells, signals are conveyed to trigger metabolic changes or reactions, such as respiration, or to suppress reactions, and gene expression and inhibition are controlled. These function as a complex network composed of many individual elements. Some elements also belong to other networks, and these networks affect each other in a complex layered structure. Systems biology models how individual elements interrelate and behave in a biological system, and uses computer simulations to verify these models.

Yoshida How are computer used effectively in systems biology?

Inoue We are discovering a great deal about how genes work, and producing an enormous amount of data. Computers are essential for handling this huge volume of data, but there are still many "missing links", that is, gaps in our understanding, that prevent us from being able to integrate this data into a cohesive whole.

Yoshida That's why using computers to draw inferences and discover hypotheses is important. Do you have any specific examples?

Inoue One example would be the mechanism for cancer resulting from ultraviolet light, for instance. When exposed to ultraviolet light, the skin's DNA gets damaged. If the number of abnormal skin cells increases, it may lead to cancer, so the body has an inhibitor gene, p53. p53 plays the essential role, but in actuality there are many reactions chained together, and if p53 binds with another protein and mutates, it may actually promote cancer formation. This structure is complex, and if the control network is completed we may be able to discover a new cancer inhibitor gene.

Yoshida Lastly, please tell us about your future goals.

Inoue The ultimate goal in this type of research is the discovery of useful hypotheses that have been heretofore unknown. In order for this to happen, the system must be used far and wide. Talking to biology researchers, I get the impression that they feel the need to process large volumes of data, but they are not sufficiently aware of systems biology. With systems biology, which handles large volumes of data, hypothesis finding systems can serve as effective tools for discovering hidden mechanisms. If there are more opportunities for the use of these systems in the future, I think they will ultimately produce results.

*1 Abduction: Used in logic to refer to inferring an explanatory hypothesis.
*2 Induction: Inference of general rules from cases. As with abduction, induction is another form of inference under incomplete knowledge.
*3 SOLAR: A system for efficiently deriving conclusions from a collection of given knowledge (logical formulas). These can be transformed to infer missing knowledge (hypotheses) from conclusions.

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Comment from the Interviewer

I thought inference and hypotheses were the exclusive domain of humans. However, computers have increased both their speed and precision. Might there be no room for humans in the future? Professor Inoue clearly dispelled that worry. "There will always be a place for humans, looking at things from a bigger picture, and getting hints from different places." Those are words born from research into areas that are tied to the very essences of computation, intelligence and life. As we unravel ever more about the systems called "biological processes", I'm certain their profundity and splendor will become even more apparent.