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### Rationality in discovery

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# Part I Introduction

What is the rational use of theory and experiment in the process of scientific discovery, in theory and in practice? In this thesis I address this problem in three parts. I start with a general **introduction** (part I). Then I discuss three different theoretical models of the process of scientific **discovery** (part II). I finish this thesis with a discussion of a case study and model of discovery in the practice of **neuropharmacology** (part III).

In this first part I provide an introduction and overview of this thesis. I start with a specification of the **problem** (Chapter 1). Then as an introduction to part two I discuss some issues and views in the study of scientific **rationality** (Chapter 2). I finish this part with an introduction and overview of discovery in **neuropharmacology** (Chapter 3).



# Chapter 1

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## Problem

### 1.1 Introduction

In this chapter I introduce the research problems about rationality in the process of scientific discovery that I faced in the years during my Ph.D. project and that are addressed in this thesis. To understand these subjects I studied different disciplines such as philosophy of science, cognitive psychology and artificial intelligence. An important problem for those disciplines is to understand what it means to be rational in the use and development of knowledge about the world.

It turns out that it is difficult to understand how we use common sense knowledge in everyday problems. I imagined that it would be less difficult to understand how scientific knowledge is used and developed. Common sense knowledge is almost by definition implicit, and therefore hard to understand. So, my idea was: why not concentrate on analyzing rationality in knowledge development that is supposed to be explicit, *i.e.* science?

So, I investigated different theories about rationality in discovery and the practice of discovery in neuropharmacology as a case study. This thesis presents the results of that investigation. I had to learn that while the product of scientific discovery is made explicit, the process of reasoning in the practice of discovery is often as implicit as common sense reasoning. So, I set myself the task to make it explicit, to understand rationality in discovery.

### 1.2 Goal

The specific goal of this thesis is to understand rationality in scientific discovery. Discovery is the act or process of making something known. Some scientific discoveries are made by accident, as a result of serendipity. But a goal of science is to make new discoveries by making use of theories and experiments to make things known. Theories are elaborate hypothetical assumptions, and experiments involve making specific observations of, and interventions in, natural phenomena. So, the method of scientific discovery is to make something known about the world with the use of theory and experiment.

To describe and understand the rationality in the process of scientific discovery I delve into the question of how acts in that process are suggested by reason. If an act is suggested by reason then there are arguments for doing something in that particular way, to achieve a particular goal. In sum, to understand rationality in scientific discovery I need to ask what it means to rationally use theory and experiment in the process of discovery in science.

### 1.3 Problem

To understand rationality in scientific discovery I analyzed different theories about the rational use of theory and experiment in science, and the practice of drug research for Parkinson's disease as a case study. An answer to the following specific problem is pursued:

**Problem** What is the rational use of theory and experiment in the process of scientific discovery, in theory and in the practice of drug research for Parkinson's disease?

An answer to this problem should provide an answer to the following specific questions about empirical science in general and neuropharmacology in particular:

**Question 1** What is the structure of a scientific theory? Generally this question treats properties of scientific laws, theories and concepts. I will pursue this question in general and particularly for the dopamine theory of Parkinson's disease and related biological theories and concepts.

**Question 2** What is the process of scientific reasoning? Traditionally, this question is about inference in the explanation and prediction of phenomena. I will also treat reasoning in the formation and revision of hypotheses.

**Question 3** What is the route between theory and experiment? This question is relevant for understanding discovery in empirical science in general and drug research in particular. Not only do I investigate how the results of experiments influence theory, but also how theory and known (drug) interventions direct the suggestion for experiments.

### 1.4 Method

To pursue the problem of this thesis I undertook the following tasks:

- A survey of contributions to the study of scientific rationality (Chapter 2)
- A conceptual study of models of discovery in science as proposed in studies of logic, cognition and computation (Chapters 4, 5, 6)

- A review of the literature on the brain dopamine theory of Parkinson's disease (Chapter 7).
- A case study of the practice of experimental drug and brain research at the Pharmacy Department of the Groningen University (Chapter 8)
- Modeling the dopamine theory and the studied practice of discovery (Chapter 9)
- Summarizing the results of the case study of neuropharmacology (Chapter 3)

## 1.5 Background

The structure of theories and processes of scientific reasoning are investigated normatively in logic and artificial intelligence, and descriptively in cognitive psychology. In studies of logic scientific reasoning is mainly explicated as valid deduction of consequences. Studies of both artificial intelligence and cognitive psychology understand the process of scientific discovery as a kind of human problem solving. In that view it is held that human beings can solve scientific problems because they can (learn to) manipulate symbols.

The work of Newell and Simon (1972) sees the process of problem solving essentially as a search process, based on the manipulation of symbols. They defend the idea that for a problem it is possible to define a space of possible solutions that can be searched. This search is done by heuristic rules that, given the problem (the start condition), test whether the solution (goal condition) is being approached, and adjust the search accordingly.

In both artificial intelligence and cognitive psychology this process is investigated and modeled computationally. In order to do so it is necessary that the structure of the problem and the required knowledge is made explicit in a symbolic representation. Based on that representation, heuristic search rules must be able to effectively test if the goal state is being approached and if it is rational to pursue a particular direction of search.

John Anderson (1993) proposed a unified theory of learning and problem solving to explain rational behavior. This theory contains assumptions about the nature of explicit symbolic processes of reasoning, together with assumptions about implicit statistical processes of learning.

In another discipline, that of machine learning, one approach takes effective learning as searching the shortest computer program that can describe and predict patterns in observations (Li & Vitanyi, 1994).

In the third part of this thesis I shall investigate how the rational use of theory and experiment in drug research can be seen in terms of the role a theory plays in directing the search for an experimental drug intervention. A theory can be seen as a constraint in the search space of conceptually possible interventions. The main goal of drug research is to find an intervention that satisfies given conditions best. Testing a theoretically suggested intervention experimentally can either lead to a new drug or a new theory.

To compare theories about discovery, as set out in Part II, to scientific practice I will analyze the structure of problems in neuropharmacology in Part III, modeling the process of reasoning in rational search tasks with different kinds of goals.

The discussed models of problems in neuropharmacology will be based on the work of Benjamin Kuipers, Peter Karp, Theo Kuipers and Rein Vos. Benjamin Kuipers (1994) investigated how to represent qualitative knowledge about dynamical systems as qualitative differential equations, and how to reason with them correctly. Peter Karp (1992) made a computational analysis of the structure of molecular biological knowledge and the process of hypothesis formation in biological research. Theo Kuipers (2000) investigates logical structures and heuristic patterns in scientific research and Rein Vos (1991) investigates the logic of development in drug research. They explicated the development of drugs theoretically as a systematic attempt to bring together the properties of available materials and wishes for functional properties. In discussing neuropharmacology I will describe how biological theory can be used to infer those desired properties, to infer the best intervention.

## 1.6 Overview

This section gives a short overview of the subjects and problems that are discussed and the particular questions that are answered in the other chapters of this thesis.

### Part I Introduction

The general problem of this thesis is: what is the rational use of theory and experiment in the process of scientific discovery, in theory and in practice? Part I discusses: issues in the study of rationality (Chapter 2), as an introduction to Part II; and my case study of neuropharmacology (Chapter 3), as an introduction to Part III.

#### Chapter 2 Rationality

This chapter provides an introduction to the discussion of discovery in Part II of this thesis. In that part I delve into ideas from cognitive psychology to look at issues about rationality in science that are traditionally part of the problems of the philosophy of science. The particular question that is answered in this chapter is: how can cognitive psychology contribute to the discussion about the rationality of science in the philosophy of science?

I argue that ideas from cognitive psychology in general can make a sensible contribution to debates about the rationality of science in philosophy. I make this point clear by explicating some relations between assumptions in cognitive psychology and issues in the philosophy of science.

#### Chapter 3 Neuropharmacology

This chapter is an introduction to my case study of neuropharmacology in Part III of this thesis. The particular question that is answered is: what is the rational use of theory and experiment in neuropharmacology?

This question is answered more extensively in Part III. I argue how the rational use of neurophysiological models can be modeled as goal directed reasoning about

qualitative differential equations. To understand reasoning in neuropharmacology I distinguish inference to the best intervention from inference to the best explanation. I further briefly discuss how qualitative reasoning about neurophysiological models as part of a computer supported discovery system could aid in using, understanding, and testing models about large biological systems.

## Part II Discovery

The specific problem of Part II (Discovery) is: what is the rational use of theory and experiment in the process of scientific discovery, in theory? This part discusses models of scientific discovery according to studies of: logic (Chapter 4); cognition (Chapter 5); and computation (Chapter 6).

### Chapter 4 Logic

What is rationality in discovery, according to the study of logic? Traditional philosophers of science are usually interested in what scientific discovery ought to be, and how reasoning in that process can be valid or justified. I discuss how rationality in discovery is logically understood as valid reasoning, part of a circular process of observing, describing, explaining, predicting and intervening in natural phenomena. The particular questions that are answered in this chapter are: what is a scientific theory and what is scientific reasoning, according to the study of logic?

To address these questions I discuss an illustrative example of an explanation that contains a series of inferences that can be marked as fallacies from the viewpoint of logic. Yet, I argue that these inferences are common in science and part of abductive inference as defined by C.S. Peirce. I further make a categorical distinction between semantic abduction and material abduction. I argue how material abduction, together with other types of inductive inference, constitutes a part of semantic abduction. I conclude by answering the three specific questions (from section 1.3) of this thesis, from a logical point of view.

### Chapter 5 Cognition

What is rationality in discovery, according to the psychological study of cognition? In cognitive psychology, rationality in scientific discovery is being studied as an interesting cognitive phenomenon, to be studied empirically. ACT-R is the name of a unified computational theory of cognition that aims to explain the data from studies of cognition. The particular question that is answered in this chapter is: how to understand and model scientific discovery with ACT-R?

I show and argue how the ACT-R model can learn by analogy the processes of two other cognitive models of discovery, called BACON and PI. I further discuss the nature of theory and method in the different cognitive models, and the difference between the logical and psychological views on explanation and prediction. I discuss how human performance on the Wason card selection task (an often performed psychological experiment where subjects test a hypothesis) seems irrational from a logical point of view. I propose a statistical model that can demonstrate the opposite. I conclude by answering the three specific questions of this thesis, according to the psychological study of cognition.



## Chapter 6 Computation

Both the logical and the cognitive models of scientific discovery I discussed in the former chapters include a condition to prefer simple explanations. Yet these models do not show why it is rational to prefer simplicity. In Chapter 5 I discussed how the ACT-R model of cognition prefers simplicity as a consequence of a mechanism that prefers high probability. In this chapter I investigate the relation between probability and simplicity in the computational description, explanation and prediction of empirical data. The particular questions that are answered in this chapter are: how can simplicity most generally be defined and why should a simpler theory be preferred above a more complex one?

I discuss how the Minimum Description Length principle subsumes other definitions of simplicity and how the simplicity of a hypothesis can be related to the probability of its predictions. I conclude by answering the three specific questions of this thesis, according to the study of computation.

## Part III Neuropharmacology

The specific problem of Part III is: what is the rational use of theory and experiment in the process of scientific discovery, in practice? This part discusses and models my case study of drug research for Parkinson's disease, *i.e.* I investigate: how Parkinson's disease and the effect of known drugs are explained by the dopamine theory (Chapter 7); the use of theory and experiments in a practice (Chapter 8); and a computational model of both the dopamine theory and the studied practice of discovery (Chapter 9)

### Chapter 7 Theory

How are theory and experiments used in the practice of drug research for Parkinson's disease? To be able to address this problem I first survey the literature on the dopamine theory of Parkinson's disease. The particular question that is answered in this chapter is: how are Parkinson's disease and the effect of known drugs explained by theory?

I first provide a general introduction to Parkinson's disease. I then go into the basics of the dopaminergic nerve cell and the basal ganglia, which is the neural structure in the brain that partly controls voluntary movement, and how a defect in it causes Parkinsonian symptoms. I end this survey with a short overview and explanation of a selection of therapeutic drug interventions for Parkinson's disease.

### Chapter 8 Practice

How are theory and experiment used in the practice of drug research for Parkinson's disease? In this chapter I report on my interviews with researchers at the Pharmacy Department of the Groningen University. These interviews were partly conducted while witnessing their work in the laboratory.

Several techniques are being used to search for new drugs and explore the activity of the basal ganglia. The particular questions that are answered in this chapter include: how are new drugs investigated and how are experiments being used to explore and test both new drugs and assumptions about the mechanisms of the brain?

**Chapter 9 Discovery**

In this final chapter I aim to explicate rationality in the process of discovery in neuropharmacology by describing both the theory and the studied practice, using the concepts from my theoretical discussion of discovery in Part II. The particular question that is answered in this chapter is: what is rationality in discovery in the case of neuropharmacology? First I discuss the use of models to describe theories about dynamical systems. Next I describe the structure of the dopamine theory of Parkinson's disease based on those models. By analyzing the reports about the practice of neuropharmacology I explicate a number of different routes between theory and experiment. I continue with a discussion of computational models of reasoning and discovery in biology. I conclude this chapter by summarizing my answers to the three specific questions of this thesis in the case of neuropharmacology. I then conclude this thesis by arguing that an answer to these questions can contribute to understanding rationality in discovery, as well as contribute to the process of scientific discovery itself.

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