PATTERNS OF MEDICAL DISCOVERY

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1. INTRODUCTION

Here are some of the most important discoveries in the history of medicine: blood circulation (1620s), vaccination, (1790s), anesthesia (1840s), germ theory (1860s), X-rays (1895), vitamins (early 1900s), antibiotics (1920s-1930s), insulin (1920s), and oncogenes (1970s). This list is highly varied, as it includes basic medical knowledge such has Harvey's account of how the heart pumps blood, hypotheses about the causes of disease such as the germ theory, ideas about the treatments of diseases such as antibiotics, and medical instruments such as X-ray machines. The philosophy of medicine should be able to contribute to understanding of the nature of discoveries such as these.

The great originators of the field of philosophy of science were all concerned with the nature of scientific discovery, including Francis Bacon (1960), William Whewell (1967), John Stuart Mill (1974), and Charles Peirce (1931-1958). The rise of logical positivism in the 1930s pushed discovery off the philosophical agenda, but the topic was revived through the work of philosophers such as Norwood Russell Hanson (1958), Thomas Nickles (1980), Lindley Darden (1991, 2006), and Nancy Nersessian (1984). Scientific discovery has also become an object of investigations for researchers in the fields of cognitive psychology and artificial intelligence, as seen in the work of Herbert Simon, Pat Langley, and others (Langley et al., 1987; Klahr, 2000). Today, scientific discovery is an interdisciplinary topic at the intersection of the philosophy, history, and psychology of science.

The aim of this chapter is to identify patterns of discovery that illuminate some of the most important developments in the history of medicine. I have used a variety of sources to identify forty great medical discoveries (Adler, 2004; Friedman and Friedland, 1998; Science Channel, 2006; Strauss and Strauss, 2006). After providing a taxonomy of medical breakthroughs, I discuss whether there is a logic of discovery, and argue that the patterns of medical discovery do not belong to formal logic. In contrast, it is possible to identify important psychological patterns of medical discovery by which new hypotheses and concepts originate. In accord with recent developments in cognitive science, I also investigate the possibility of identifying neural patterns of discovery. Finally, I discuss the role that computers are currently playing in medical discovery.

2. MEDICAL HYPOTHESES

There are at least four different kinds of hypotheses employed in medical discovery: hypotheses about basic biological processes relevant to health; hypotheses about the causes of disease; hypotheses about the treatment of disease; and hypotheses about how physical instruments can contribute to the diagnosis and treatment of disease. Generation of new hypotheses about health and disease often involves the creation of new concepts such as *virus, vitamin C,* and *X-ray*. I will now give examples of the different kinds of medical hypotheses and concepts.

Although medicine is largely concerned with the diagnosis, causes, and treatment of disease, a great deal of medical knowledge concerns the basic biological processes that support healthy functioning of the body. The first reliable account of human anatomy was Vesalius's *On the Fabric of the Human Body,* published in 1543, which provided detailed illustrations of the structure of bones, muscles, organs, and blood vessels. His careful dissections produced discoveries about the structure of human bones that contradicted the accepted account of Galen, who had only dissected non-humans. The first major discovery in physiology was William Harvey's recognition in his 1628 book that blood circulates through the body as the result of the pumping action of the heart. Although cells were first observed in the seventeenth century, it took 200 years before the discovery and acceptance of the hypotheses that all living things are made of cells and that all cells arise from preexisting cells. During the twentieth century, many hypotheses about the functioning of the human body were generated and confirmed, establishing the fields of genetics and molecular biology that provided the basis for modern molecular understanding of the causes of health and disease. Table 1 summarizes some of the most important medical discoveries concerned with basic biological processes. All of these discoveries eventually contributed to discovery of the causes and treatments of disease, with a delay of decades or even centuries. For example, van Leeuwenhoek's discovery of "little animals" such as bacteria only became medically important 200 years later with the development of the germ theory of disease. All of these basic medical discoveries involved hypotheses about biological structure or function, and some required the introduction of new concepts such as *cell, gene,* and *hormone*.

DECADE	DISCOVERY	DISCOVERER	HYPOTHESES
1540s	anatomy	Vesalius	bone structure, etc.
1620s	circulation	Harvey	blood circulates
1670s	bacteria	Leeuwenhoek	animalcules exist
1830s	cell theory	Schleiden,etc.	organs have cells
1860s	genetics	Mendel	inheritance
1900s	hormones	Bayliss, etc.	messaging
1950s	DNA	Watson, Crick	DNA structure
1950s	immune system	Lederberg,etc.	clonal deletion

Table 1. Some major discoveries concerning medically important biological processes.

Discoveries that are more specifically medical concern the causes of diseases. Until modern Western medicine emerged in the nineteenth century, the predominant world theories attributed disease to bodily imbalances, involving the humors of Hippocratic medicine, the *yin, yang* and *chi* of traditional Chinese medicine, and the *doshas* of traditional Indian Ayurvedic medicine. Pasteur revolutionized the explanation of disease in the 1860s with the hypothesis that many diseases such as cholera are caused by bacteria. In the twentieth century, other diseases were connected with infectious agents, including viruses and prions. The nutritional causes of some diseases were identified in the early twentieth century, for example how vitamin C deficiency produces scurvy. Autoimmune diseases require explanation in terms of malfunction of the body's immune system, as when multiple sclerosis arises from damage to myelin in the central nervous system. Some diseases such as cystic fibrosis have a simple genetic basis arising from inherited mutated genes, while in other diseases such as cancer the molecular/genetic causes are more complex. The general form of a hypothesis about disease causation is: disease D is caused by factor F, where F can be an external agent such as a microbe or an internal malfunction. Table 2 displays some of the most important discoveries about the causes of diseases.

DECADE	DISCOVERY	DISCOVERER	HYPOTHESES
1840s	cholera	Snow	cholera is water-borne
1840s	antisepsis	Semmelweiss	contamination causes fever
1870s	germ theory	Pasteur, Koch	bacteria cause disease
1890s	tobacco disease	Ivanofsky, Beijerinck	viruses cause disease
1910s	cholesterol	Anichkov	cause of artherosclerosis
1960s	oncogenes	Varmus	cancer
1980s	prions	Prusiner	prions cause kuru
1980s	HIV	Gallo, Montagnier	HIV causes AIDS
1980s	H. pylori	Marshall, Warren	H. pylori causes ulcers

Table 2. Some major discoveries concerning the causes of diseases.

The third kind of medical hypothesis, and potentially the most useful, concerns the treatment and prevention of disease. Hypotheses about treatment of disease based on traditional imbalance theories, for example the use in Hippocratic medicine of bloodletting to balance humors, have been popular but unsubstantiated. In contrast, Edward Jenner's discovery in the 1790s that inoculation provides immunity to smallpox has saved millions of lives, as has the twentieth-century discoveries of drugs to counter the infectious properties of bacteria and viruses. The discovery of insulin in the 1920s provided an effective means of treating type 1 diabetes, which had previouisly been fatal. Treatments need not actually cure a disease to be useful: consider the contribution of steroids to diminishing the symptoms of autoimmune diseases, and the use of painkillers such as aspirin to treat various afflictions. Surgical treatments have often proved useful for treating heart disease and cancer.

It might seem that the most rational way for medicine to progress would be from basic biological understanding to knowledge of the causes of a disease to treatments for the disease. Often, however, effective treatments have been found long before deep understanding of the biological processes they affect. For example, aspirin was used as a painkiller for most of a century before its effect on prostaglandins was discovered, and antibiotics such as penicillin were in use for decades before it became known how they kill bacteria. Lithium provided a helpful treatment for bipolar (manic-depressive) disorder long before its mechanism of action on the brain was understood. On the other hand, some of the discoveries about causes listed in table 2 led quickly to therapeutic treatments, as when the theory that ulcers are caused by bacterial infection was immediately tested by treating ulcer patients with antibiotics (Thagard, 1999).

Table 3 lists some of the most important discoveries about medical treatments. These fall into several disparate subcategories, including prevention, surgical techniques, and drug treatments. Vaccination, antisepsis, and birth control pills serve to prevent unwanted conditions. Anesthesia, blood transfusions, organ transplants, and in vitro fertilization all involve the practice of surgery. Drug treatments include aspirin, antibiotics, and insulin. All of the treatments in table 3 are based on hypotheses about how an intervention can bring about improvements in a medical situation. A few involve new concepts, such as the concept of a blood type which was essential for making blood transfusions medically feasible.

DECADE	DISCOVERY	DISCOVERER	HYPOTHESES
1790s	vaccination	Jenner	prevent smallpox
1840s	anesthesia	Long	reduce pain
1860s	antiseptic surgery	Lister	prevent infection
1890s	aspirin	Hoffman	treat pain
1890s	radiation treatment	Freund	remove cancer
1900s	Salvarsan	Ehrlich	cure syphilis
1900s	blood transfusion	Landsteiner	transfusion works
1920s	antibiotics	Fleming	mold kills bacteria
1920s	insulin	Banting	treat diabetes
1930s	sulfa drugs	Domagk	cure infection
1950s	birth control pill	Pincus, etc.	prevent pregnancy
1950s	transplants	Murray	kidney, lung
1950s	polio vaccination	Salk	prevent polio
1960s	IVF	Edwards	treat infertility
1980s	anti-retrovirals	various	slow HIV infection

Table 3. Some major discoveries about treatments of diseases.

My fourth kind of medical discovery involves hypotheses about the usefulness of various instruments. I listed X-rays among the most important medical discoveries because of the enormous contribution that X-ray machines have made to diagnosis of many ailments, from bone fractures to cancers. Other instruments of great medical importance are the stethoscope, invented in 1816, and techniques of testing blood for blood type, infection, and other medically relevant contents such as cholesterol levels. More recent instruments of medical significance include ultrasound scanners developed in the 1960s, computed tomography (CT) scanners invented in the 1970s, and magnetic resonance imaging (MRI) adopted in the 1980s. All of these instruments required invention of a physical device, which involved hypotheses about the potential usefulness of the device for identifying diseases and their causes. Table 4 lists some of the major medical discoveries involving physical instruments useful for the diagnosis of diseases. The origination of such instruments is perhaps better characterized as *invention* rather than discovery, but it still requires the generation of new hypotheses about the effectiveness of the instrument for identifying normal and diseased states of the body. For example, when Laennec invented the stethoscope, he did so because he hypothesized that a tube could help him better hear the operation of his patients' hearts.

DECADE	DISCOVERY	DISCOVERER	HYPOTHESES
1810s	stethoscope	Laennec	measure heart
1890s	x-rays	Reontgen	reveal bones
1900s	EKG	Einthoven	measure heart
1900s	tissue culture	Harrison	detect infections
1920s	cardiac catheterization	Forssman	inspect heart
1950s	radioimmunoassay	Yalow	analyze blood
1970s	CAT scans	Hounsfield	observe tissue
1970s	MRI scans	Lauterbur	observe tissue

Table 4. Some major discoveries of diagnostic instruments.

The discovery of new hypotheses always requires the novel juxtaposition of concepts not previously connected. For example, the hypotheses that comprise the germ theory of disease connect a specific disease such as peptic ulcer with a specific kind of bacteria such as Helicobacter pylori. Construction of hypotheses requires the application and sometimes the generation of concepts. In the early stage of the bacterial theory of ulcers, Barry Marshall and Robin Warren associated the concepts *ulcer, cause,* and *bacteria*, and later their hypothesis was refined by specification of the bacteria via the concept of *H. pylori*. Other concepts of great importance in the history of discovery of the causes of disease include *vitamin, virus, autoimmune, gene,* and *oncogene*. Hence a theory of medical discovery will have to include an account of concept formation as well as an account of the generation of hypotheses. How this might work is discussed in the section below on psychological patterns.

All the medical discoveries so far discussed have involved the generation of specific new hypotheses. But there is another kind of more general medical breakthrough that might be counted as a discovery, namely the development of new methods for investigating the causes and treatments of disease. Perhaps the first great methodological advance in the history of medicine was the Hippocratic move toward natural rather than magical or theological explanations of disease. The theory of humors was not, as it turned out millennia later, a very good account of the causes and treatments of disease, but at least it suggested how medicine could be viewed as akin to science rather than religion. In modern medicine, one of the great methodological advances was Koch's postulates for identifying the causes of infectious diseases (Brock 1988, p. 180):

1) The parasitic organism must be shown to be constantly present in characteristic form and arrangement in the diseased tissue.

2) The organism which, from its behavior appears to be responsible for the disease, must be isolated and grown in pure culture.

3) The pure culture must be shown to induce the disease experimentally.

It turned out that these requirements, identified by Koch in the 1870s as part of his investigation of tuberculosis, are sometimes too stringent a requirement for inferring causes of infectious diseases, because some infectious agents are extremely difficult to culture and/or transmit. But the postulates have been useful for setting a high standard for identifying infectious agents. A third methodological breakthrough was the use, beginning only in the late 1940s, of controlled clinical trials in the investigation of the efficacy of medical treatments. Only decades later was it widely recognized that medical practices should ideally be determined by the results of randomized, double-blind, placebo-controlled trials, with the emergence of the movement for evidence-based medicine in the 1990s. None of these three methodological breakthroughs involve the discovery of particular medical hypotheses, but they have been crucial to development of well-founded medical views about the causes and treatments of diseases.

3. LOGICAL PATTERNS

Karl Popper published the English translation of his *Logik der Forschung* with the title *The Logic of Scientific Discovery*. The title is odd, for in the text he sharply distinguishes between the process of conceiving a new idea, and the methods and results of examining it logically (Popper, 1959, p. 21). The book is concerned with logic, not discovery. Like Reichenbach (1938) and many other philosophers of science influenced by formal logic, Popper thought philosophy should not concern itself with psychological processes of discovery. The term "logic" had come to mean "formal logic" in the tradition of Frege and Russell, in contrast to the broader earlier conception of logic as the science and art of reasoning. In John Stuart Mill's (1970/1843) *System of Logic,* for example, logic is in part concerned with the mental processes of reasoning, which include inferences involved in scientific discovery.

If logic means just "formal deductive logic", then there is no logic of discovery. But N. R. Hanson (1958, 1965) argued for a broader conception of logic, which could be concerned not only with reasons for accepting an hypothesis but also with reasons for entertaining a hypothesis in the first place. He borrowed from Charles Peirce the idea of a kind of reasoning called *abduction* or *retroduction,* which involves the introduction of hypotheses to explain puzzling facts. By abduction Peirce meant "the first starting of a hypothesis and the entertaining of it, whether as a simple interrogation or with any degree of confidence" (Peirce 1931-1958, vol. 6, p. 358). Unfortunately, Peirce was never able to say what the first starting of a hypothesis amounted to, aside from speculating that people have an instinct for guessing right. In multiple publications, Hanson only managed to say that a logic of discovery would include a study of the inferential moves from the recognition of an anomaly to the determination of which types of hypothesis might serve to explain the anomaly (Hanson, 1965, p. 65). Researchers in artificial intelligence have attempted to use formal logic to model abductive reasoning, but Thagard and Shelley (1997) describe numerous representational and computational shortcomings of these approaches, such as that explanation is often not a deductive relation.

The closest we could get to a logical pattern of hypothesis generation for medical discovery, in the case of disease, would be something like:

Anomaly: People have disease D with symptoms S.

Hypothesis: Cause C can produce S.

Inference: So maybe C is the explanation of D.

For Pasteur, this would be something like:

Anomaly: People have cholera with symptoms of diarrhea, etc.

Hypothesis: Infection by a bacterium might cause such symptoms.

Inference: So maybe bacterial infection is the explanation of cholera.

Unfortunately, this patterns leaves unanswered the most interesting question about the discovery: how did Pasteur first come to think that infection by a bacterium might cause cholera? Answering this question requires seeing abduction as not merely a kind of deformed logic, but rather as a rich psychological process.

For Popper, Reichenbach, and even Hanson and Peirce, there is a sharp distinction between logic and psychology. This division is the result of the schism between philosophy and psychology that occurred because of the rejection by Frege and Husserl of psychologism in philosophy, as inimical to the objectivity of knowledge (see Thagard, 2000, ch. 1, for a historical review). Contemporary naturalistic epistemology in the tradition of Quine (1968) and Goldman (1986) rejects the expulsion of psychology from philosophical method. I will now try to show how richer patterns in medical discovery can be identified from the perspective of modern cognitive psychology.

4. PSYCHOLOGICAL PATTERNS

We saw in the last section that little can be said about discovery from the perspective of a philosophy of science that emphasizes logical structure and inference patterns. In contrast, a more naturalistic perspective that takes into account the psychological processes of practicing scientists has the theoretical resources to explain in much detail how discoveries come about. These resources derive from the development since the 1960s of the field of cognitive psychology, which studies the representations and procedures that enable people to accomplish a wide range of inferential tasks, from problem solving to language understanding. Starting in the 1980s, some philosophers of science have drawn on cognitive science to enrich accounts of the structure and growth of science knowledge (see e.g. Carruthers, Stich, and Seigal, 2002; Darden, 1991, 2006; Giere, 1988; Nersessian, 1992; Thagard, 1988, 1992, 1999). On this view, we should think of a scientific theory as a kind of mental representation that scientists can employ for many purposes such as explanation and discovery. Then scientific discovery is the generation of mental representations such as concepts and hypotheses.

I will not attempt a comprehensive account of all the cognitive processes relevant to discovery, nor attempt to apply them to explain the large number of discoveries listed in tables 1-4. Instead I will review a cognitive account of a single major medical discovery, the realization by Barry Marshall and Robin Warren that most stomach ulcers are caused by bacterial infection, for which they were awarded the 2005 Nobel Prize in Physiology or Medicine. Figure 1 depicts a general model of scientific discovery developed as part of my account of the research of Marshall and Warren (Thagard, 1999). Discovery results from two psychological processes, questioning and search, and from serendipity. Warren's initial discovery of spiral gastric bacteria was entirely serendipitous, happening accidentally in the course of his everyday work as a pathologist. Warren reacted to his observation of these bacteria with surprise, as it was generally believed that bacteria could not long survive the acidic environment of the stomach. This surprise, along with general curiosity, led him to generate questions concerning the nature and possible medical significance of the bacteria.

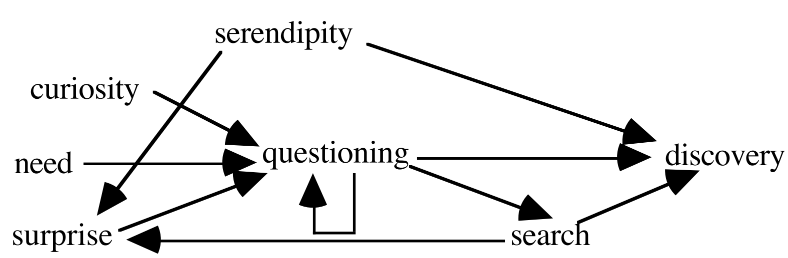

Figure 1. Psychological model of discovery. From Thagard (1999), p. 47.

Warren enlisted a young gastroenterologist, Barry Marshall, to help him search for answers about the nature and medical significance of the spiral bacteria. After an extensive examination of the literature on bacteriology, they concluded that the bacteria were members of a new species and genus, eventually dubbed *Helicobacter pylori*. Here we see the origin of a new concept, that is a mental representation of the bacteria that Warren observed through a microscope. Marshall's questioning about the medical significance of these bacteria was driven, not only by curiosity, but also by medical needs, as he was aware that available medical treatments for stomach ulcers using antacids were not very effective, diminishing symptoms but not preventing recurrences.

Warren had observed that the bacteria were associated with inflammation of the stomach (gastritis), and Marshall knew that gastritis is associated with peptic ulcer, so they naturally formed the hypothesis that the bacteria might be associated with ulcers. A 1982 study using endoscopy and biopsies found that patients with ulcers were far more likely to have *H. pylori* infections than patients without ulcers. They accordingly generated the hypothesis that the bacteria cause ulcers, by analogy with the many infectious diseases that had been identified since Pasteur. The natural psychological heuristic used here is something like: if A and B are associated, then A may cause B or vice versa. In order to show that A actually does cause B, it is desirable to manipulate A in a way that produces a change in B. Marshall and Warren were initially stymied, however, because of difficulties in carrying out the obvious experiments of giving animals *H. pylori* to induce ulcers and of giving people with ulcers antibiotics to try to kill the bacteria and cure the ulcers. Within a few years, however, they had discovered a regime involving multiple antibiotics that was effective at eradicating the bacteria, and by the early 1990s there were multiple international studies that showed that such eradication often cured ulcers.

The discoveries of Marshall and Warren involve two main kinds of conceptual change. The first kind was introduction of the new concept of *Helicobacter pylori,* which was the result of both perceptual processes of observing the bacteria and of cognitive processes of conceptual combination. Originally they thought that the bacteria might belong to a known species, *Campylobacter,* hence the original name *Campylobacter pylori,* signifying that the new species inhabited the pylorus, the part of the stomach that connects to the duodenum. However, morphological and RNA analysis revealed that the new bacteria were very different from *Campylobacter,* so that they were reclassified as members of a new genus. Such reclassification is a second major kind of conceptual change, in that the discovery that bacteria cause ulcers produced a dramatic reclassification of the peptic ulcer disease. Previously, ulcers were viewed as metabolic diseases involving acid imbalance, or even, in older views as being psychosomatic diseases resulting from stress. Through the work of Marshall and Warren, peptic ulcers (except for some caused by non-steroidal anti-inflammatory drugs such as aspirin) were reclassified as infectious diseases, just like tuberculosis and cholera.

Thus the discovery of the bacterial theory of ulcers involved the generation and revision of mental representations. New concepts such as *H. pylori* were formed, and conceptual systems for bacteria and diseases were reorganized. Also generated were hypotheses, such as that bacteria cause ulcers and that ulcers can be treated with antibiotics. Both these sorts of representations can be produced by psychological processes of questioning, search, conceptual combination, and causal reasoning.

Analogy is a psychological process that often contributes to scientific discovery (Holyoak and Thagard, 1995). Marshall and Warren reasoned analogically when they thought that ulcers might be like more familiar infectious diseases. Other analogies have contributed to medical discoveries, such as Semmelweiss' mental leap from how a colleague became sick as the result of a cut during an autopsy to the hypothesis that childbed fever was being spread by medical students. Thagard (1999, ch. 9) describes other analogies that have contributed to medical discoveries, such as Pasteur's realization that disease is like fermentation in being caused by germs, and Funk's argument that scurvy is like beriberi in being caused by a vitamin deficiency. Thus analogy, like questioning, search, concept formation, and causal reasoning is an identifiable psychological pattern of discovery applicable to medical innovations.

5. NEURAL PATTERNS

The field of cognitive psychology is currently undergoing a major transformation in which the study of brain processes is becoming more and more central. Psychologists have long assumed that mental processing was fundamentally carried out by the brain, but the early decades of cognitive psychology operated independently of the study of the brain. This independence began to evaporate in the 1980s with the development of brain scanning technologies such as fMRI machines that enabled psychologists to observe brain activities in people performing cognitive tasks. Another major development in that decade was the development of connectionist computational models that used artificial neural networks to simulate psychological processes. (For a review of approaches to cognitive science, see Thagard 2005). As illustrated by many journal articles and even the title of a recent textbook, *Cognitive Psychology: Mind and Brain* (Smith and Kosslyn, 2007), the field of cognitive science has become increasingly connected with neuroscience.

This development should eventually yield new understanding of scientific discovery. The psychological patterns of discovery described in the last section saw it as resulting from computational procedures operating on mental representations. From the perspective of cognitive neuroscience, representations are processes rather than things: they are patterns of activity in groups of neurons that fire as the result of inputs from other neurons. The procedures that operate on such mental representations are not much like the algorithms in traditional computer programs that inspired the early computational view of mind. Rather, if mental representations are patterns of neural activity, then procedures that operate on them are neural mechanisms that transform the firing activities of neural groups.

Accordingly, we ought to be able to generate new patterns of medical discovery construed in terms of neural activity. To my knowledge, the only neural network model of discovery is a highly distributed model of abductive inference described by Thagard and Litt (2008). They showed how to implement in a system of thousands of artificial neurons the simple pattern of inference from the occurrence of puzzling occurrence A and the knowledge that B can cause A to the hypothesis that B might have occurred. Representation of A, B, and *B causes A,* is accomplished, not by a simple expression or neuron, but by the firing activity of neural groups consisting of hundreds or thousand of neurons. The inference that B might have occurred is the result of systematic transformations of neural activity that take place in the whole system of neurons. This simple kind of abductive inference is not sufficient to model major medical discoveries, but it does appear appropriate for diagnostic reasoning of the following sort common in medical practice: this patient has ulcers, ulcers can be caused by bacterial infection, so maybe this patient has a bacterial infection. Much work remains to be done to figure out how neural systems can perform more complex kinds of inference, such as those that gave rise in the first place to the bacterial theory of ulcers.

On the neuroscience view of mental representation, a concept is a pattern of neural activity, so concept formation and reorganization are neural processes. In the development of the bacterial theory of ulcers, initial formation by Warren of the concept of spiral gastric bacteria seems to have been both perceptual and cognitive. The perceptual part began with the stimulation of Warren's retina by light rays reflected from his slides of stomach biopsies that revealed the presence of bacteria. At that point his perceptual representation of the bacteria was presumably a visual image constituted by neural activity in the brain's visual cortex. Warren's brain was able to integrate that visual representation with verbal representations consisting of other neural activities, thus linking the visual image to the verbal concepts *spiral, gastric,* and *bacteria*. But these concepts are not simply verbal, since they also involve representations that are partly visual, as is particularly obvious with the concept *spiral*. It is likely that for an experienced pathologist such as Warren the concepts *gastric* and *bacteria* are also partially visual: he had often seen pictures and diagrams of organs and microorganisms.

So how does the brain form concepts such as *spiral gastric bacteria of the kind observed through the microscope in Warren's samples?* I have previously described generation of new concepts as a kind of verbal conceptual combination, such as production of *sound wave* by combining the concepts of *sound* and *wave* (Thagard, 1988). But the neural process for Warren's new concept is considerably more complicated, as it requires integrating multiple representations including both verbal and nonverbal aspects. Here is a sketch of how this neural process might operate.

A crucial theoretical construct in cognitive psychology and neuroscience is *working memory* (Smith and Kosslyn, 2007; Fuster, 2004). Long term memory in the brain consists of neurons and their synaptic connections. Working memory is a high level of activity in those groups of neurons that have been stimulated to fire more frequently by the current perceptual and inferential context that a person encounters. Then conceptual combination is the co-occurrence and coordination in working memory of a number of perceptual and verbal representations, each of which consists of patterns of neural activity. It is not yet well understood how this coordination occurs, but plausible hypotheses include neural synchronization (the patterns of neural activity become temporally related) and higher-level representations (patterns of neural activity in other neural groups represent patterns in the neural groups whose activity represents the original concepts). These two hypotheses may be compatible, since something like temporal coordination may contribute to the neural activity of the higher-order concept that ties everything together. Thus concept formation by perceptual-conceptual combination is a neural process involving the simultaneous activation and integration of previously unconnected patterns of neural activity.

This new account of multimodal conceptual combination goes well beyond the symbolic theory that I have applied to scientific discovery (Thagard, 1988). As Barsalou, et al. (2003) argue, conceptual representations are often grounded in specific sensory modalities. For example, the concept *brown* is obviously connected with visual representation, as are more apparently verbal concepts like *automobile,* which may involve auditory and olfactory representations as well as visual ones. One advantage of theorizing at the neural level is that all of these kinds of verbal and sensory representations have the same underlying form: patterns of activity in neural groups. Hence newly generated concepts such as *brown automobile* and, more creatively, *gastric spiral bacteria,* can consist of neural activities that integrate verbal and sensory representations.

6. TECHNOLOGICAL PATTERNS

My discussion of logical, psychological, and neural patterns of medical discovery has so far concerned the contributions of human beings to medical advances. But medical research is increasingly relying on computers, not only to store information about biological systems but also to help generate new hypotheses about the causes and cures of disease. This section briefly sketches some emerging patterns of discovery that involve interactions between people and computers.

Computers have been essential contributors to projects involving basic biological processes, such as the Human Genome Project completed in 2003. This project succeeded in identifying all the 20,000-25,000 genes in human DNA, determining the sequences of the 3 billion base pairs that make up human DNA, and storing the information in computer databases (Human Genome Project, 2006). All diseases have a genetic component, whether they are inherited or the result of an organism's response to its environment. Hence the information collected by the Human Genome Project should be of great importance for future investigations into the causes and treatments of a wide range of diseases. Such investigations would not be possible without the role of computers in sequencing, storing, and analyzing DNA information.

GenBank, the genetic sequence database compiled by the U. S. National Institutes of Health, contains over 50 million sequence records. These records include descriptions of many viruses, which proved useful in identifying the cause of the disease SARS that suddenly emerged in 2003. Within a few months, scientists were able to use the GenBank information and other technologies such as microarrays to determine that the virus responsible for SARS is a previously unidentified coronoavirus (Wang, et al., 2003). Without computational methods for identifying the DNA structure of the virus associated with SARS and for comparing it with known structures, knowledge of the cause of SARS would have been greatly limited. Thus computers are beginning to contribute to understanding of the causes of human diseases.

New technologies are also being developed to help find treatments for disease. Robots are increasingly used in automated drug discovery as part of the attempt to find effective new treatments, for example new antibiotics that are not resistant to existing treatments. Lamb et al. (2006) describe their production of a "connectivity map", a computer-based reference collection of gene-expression profiles from cultured human cells treated with bioactive small molecules, along with pattern-matching software. This collection has the potential to reveal new connections among genes, diseases, and drug treatments. Thus recent decades have seen the emergence of a new class of patterns of medical discovery in which human researchers cooperate with computers. Scientific cognition is increasingly distributed, not only among different researchers, but also among researchers and computers with which they interact (Thagard, 1993, 2006; Giere, 2002). Because medical discovery is increasingly a matter of distributed cognition, the philosophy of medicine needs to investigate the epistemological implications of the collaborative, techological nature of medical research.

7. CONCLUSION

Although not much can be said about the *formal* logic of medical discovery, I hope to have shown that discovery is a live topic in the philosophy of medicine. We have seen that there are four kinds of discovery that require investigation, concerning basic biological processes, the causes of disease, the treatment of disease, and the development of new instruments for diagnosing and treating diseases. Psychological patterns of discovery include the development of new hypotheses by questioning, search, and causal reasoning, and the development of new concepts by combining old ones. Research in the burgeoning field of cognitive neuroscience is making it possible to raise, and begin to answer, questions about the neural processes that enable scientists to form hypotheses and generate concepts. In addition, philosophers can investigate how computers are increasingly contributing to new medical discoveries involving basic biological processes and the causes of disease. A major aim of the philosophy of medicine is to explain the growth of medical knowledge. Developing a rich, interdisciplinary account of the patterns of medical discovery should be a central part of that explanation.

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