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SCIENTIFIC REASONING STRATEGIES IN A SIMULATED MOLECULAR GENETICS ENVIRONMENT

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ABSTRACT

Two studies are reported investigating the strategies that subjects use to revise hypotheses following disconfirmation. Subjects attempted to discover how genes are controlled by conducting experiments in a simulated molecular genetics laboratory. In Study 1, subjects set a goal of finding an experimental result, when this goal was not achieved they adopted one of the three following strategies. (1) Distort the logic of evidence interpretation to fit the current goal. (2) Conduct a parametric analysis of the Experiment space to achieve the goal. (3) Set a new experimental goal of trying to discover the cause of unexpected findings. Only the third group discovered how the genes are controlled. In Study 2, the hypothesis that the subject's experimental goal blocks consideration of alternative hypotheses was investigated. When subjects were allowed to reach their initial goal, they then set a new goal of accounting for unusual findings and discovered the mechanism of control. These results suggest that the goal of the subjects constrains search of both an Hypothesis and an Experiment space. This strategy can produce distortions in reasoning and a failure to generate new hypotheses.

One of the most interesting paradoxes in research on human reasoning is that subjects and scientists alike tend to seek evidence that confirms and ignore evidence that disconfirms their hypotheses, yet both subjects and scientists discover concepts and make scientific progress. While many researchers have argued that these strategies are inappropriate (e.g., Popper, 1959; Wason, 1960; Mynatt, Doherty, & Tweney, 1977), others have argued that when the probability of having one's hypothesis disconfirmed is high, a useful strategy is to seek confirmation. This latter view is based on the premise that disconfirming evidence can be used to guide formation of new hypotheses and generation of new experiments (cf. Dunbar & Klahr, 1989; Klahr & Dunbar, 1988; Klayman & Ha, 1987). While Klayman and Ha have demonstrated that this strategy is statistically appropriate when the predominant experimental outcome is disconfirmation, the cognitive strategies for dealing with disconfirming evidence are unknown. The purpose of the two studies reported here is to investigate hypothesis revision and subsequent experimentation following the disconfirmation of initial hypotheses.

A further goal of this research is to investigate scientific reasoning strategies in a task that more closely resembles real scientific reasoning. As we have argued elsewhere (Dunbar & Klahr, 1989; Klahr & Dunbar, 1988) many of the tasks that have been used to study scientific reasoning involve arbitrary experiments (e.g., pick this card, generate a sequence of numbers), and arbitrary hypotheses (e.g., all cards with one border, numbers of increasing magnitude). While these studies have provided many insights into the reasoning strategies that subjects use, they involve little prior knowledge and the to-be-discovered concept is an arbitrary concatenation of features.

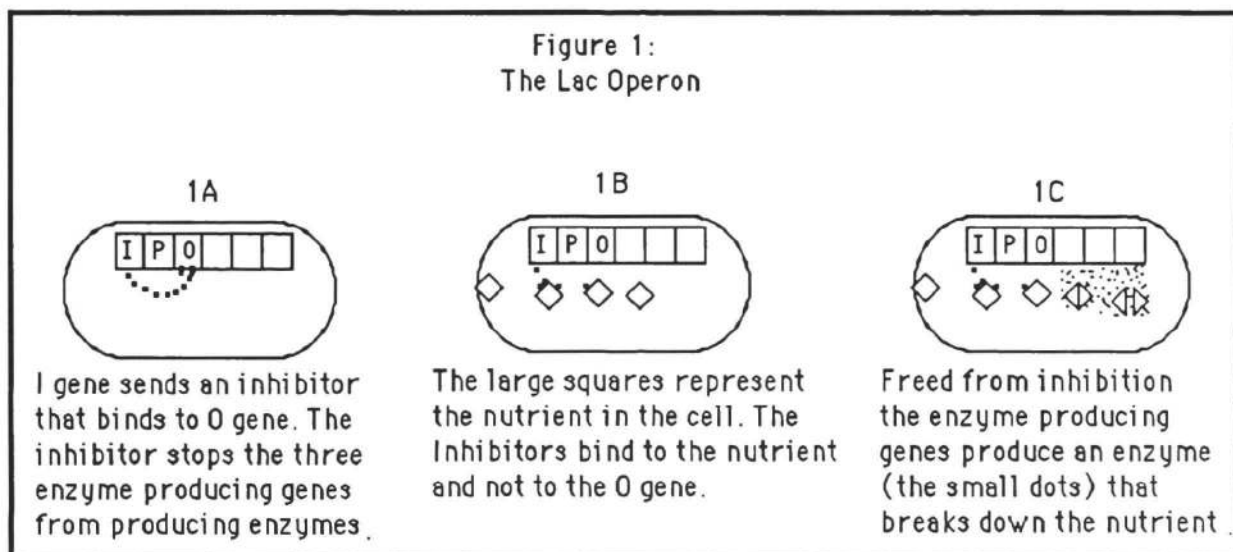
In the studies reported below, a different approach to scientific reasoning is taken: subjects must propose hypotheses and conduct experiments in a real scientific domain -- molecular genetics. Subjects were given the task of discovering the mechanism by which genes are controlled by other genes. This particular problem has been of central concern to molecular biologists for the past forty years, and provides an interesting domain within which to investigate scientific reasoning. Using this task, subjects were given some initial knowledge about the

domain and a number of experimental tools that are similar to those used in genetics laboratories. This task makes it possible to investigate the cognitive processes that are involved in scientific reasoning and more particularly the nature of hypothesis revision and experimentation following disconfirmation.

The Molecular Genetics domain. One of the major events in science of this century has been the founding of molecular genetics. The most well-known breakthrough in this field being the discovery of the structure of DNA by Watson and Crick in 1953. This field has had many other discoveries that are at the core of current day theorizing about genetics. One such discovery was the mechanisms by which genes are controlled (Jacob & Monod, 1961). Monod and Jacob discovered that some genes control the functioning of other genes and specified the mechanisms by which this control occurs. Because of the major importance of this finding, Jacob and Monod were awarded the Nobel Prize in 1965.

Monod and Jacob demonstrated that in the bacterium *ecoli*, there are regulator genes that control the activity of other genes. This mechanism of genetic control is known as the Lac Operon. *Ecoli* need glucose to live and one of the common sources of glucose for *ecoli* is lactose. When there is lactose present the *ecoli* secrete enzymes that break down the lactose into glucose. The *ecoli* can then use the glucose as an energy source. The *ecoli* only secrete the enzymes that breakdown the lactose when the lactose is present. When there is no lactose present the enzymes are not secreted. The question that Monod and Jacob investigated was how the *ecoli* regulates its activity so that it only secretes enzymes when lactose is present. They discovered that the regulator genes inhibit the production of various enzymes until the enzymes are needed. The details of the mechanism are given below in Figure 1.

Simulating molecular genetics in the cognitive laboratory. The work of Monod and Jacob provides an interesting problem that can be transposed to the psychological laboratory and subjects can be given the task of discovering the mechanisms of genetic control. Thus rather than inventing an arbitrary task that embodies certain aspects of science it is possible to give subjects a real scientific problem to work with. In the studies presented below, subjects were taught about genetics and shown how to conduct simulated molecular genetics experiments on the computer, and then were asked to discover how the genes were controlled. The task that the subjects were presented with was to discover the Lac Operon. Note that the purpose of this work is not to simulate the way in which Monod and Jacob discovered the Lac Operon, but to use a task that involves some real scientific concepts and experimentation to address the cognitive components of the scientific discovery process.

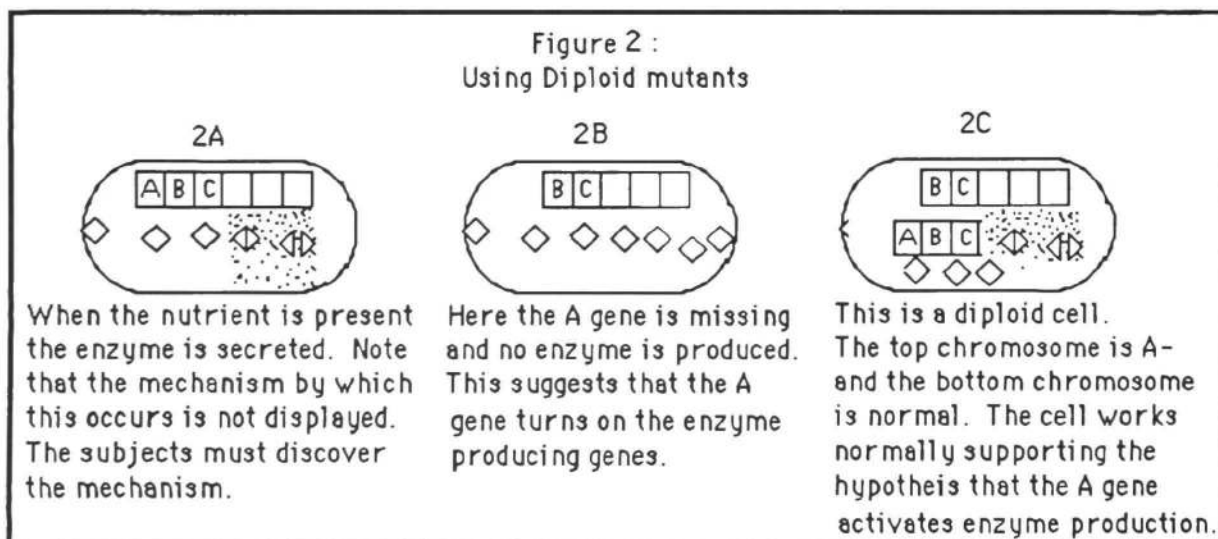


Standard Experimental Procedure. Subjects were trained in some of the very elementary concepts of molecular genetics on a MacIntosh II computer. The display was highly interactive: subjects conducted experiments by pulling down menus and selecting various options from the menus. Once the experiment was designed subjects could run the experiment to see what happens. The screen display was similar to that displayed in Figures 1 and 2. However, unlike figure 1, subjects could not see any genes secreting inhibitors and activators, they had to induce this concept from experimental results. Subjects learned that chromosomes consist of genes and that the genes have particular functions. Subjects were told that certain genes control the activities of other genes by switching them on when there is a nutrient present. This is an example of activation -- the controller gene senses that there is a nutrient present and then releases substances that instruct other genes to secrete enzymes that can utilize the nutrient.

Subjects were shown how to conduct simulated experiments that allowed them to determine how the controller genes switch on the other genes. These experiments were conducted using three controller genes A, B, and C that are attached to three enzyme producing genes (see Figure 2A). Subjects were taught a number of standard techniques for discovering the functions of the genes.

The first technique was specifying the amount of nutrient given (zero, 100, 200, 300, 400 and 500 microgrammes). The second technique was using various types of genetic mutations. One type of mutant is haploid. Normal haploid ecoli have the A, B, C, and enzyme producing genes present. Mutant haploid ecoli have either the A, B, or C genes missing. Only one gene can be removed at a time. For example in Figure 2B the A gene is missing. Diploid ecoli have two chromosomes. The normal diploid has the A, B, C, and enzyme producing genes on one chromosome, and has a second chromosome that has the A, B, and C genes on it. In diploid mutants one chromosome may have a gene missing (as in Figure 2C), or both chromosomes may have a gene missing. As can be seen from figure 2, Diploid ecoli can be used to discover the mechanisms of control: if a gene is missing from one chromosome and is present on the other chromosome the ecoli may now work normally. In figure 2 this suggests activation. Other experimental results might suggest inhibition.

The third component of experimentation was monitoring the output of the enzyme. After every experiment the subjects saw a table of results showing whether the ecoli was haploid or diploid, what mutations were made (i.e., what genes were missing), how much nutrient was added, and how much enzyme was produced. This data was displayed in a table that appeared after every experiment. This table also contained the results of all previous experiments. After subjects had learned to use these techniques they were given some problems that demonstrated that they understood the theoretical concepts and experimental techniques that they had learned.



In the second part of the study, subjects were presented with two findings about a set of genes and were asked to discover how the enzyme producing genes are controlled. The genes were very similar to the learning experience for the A, B, and C genes. In this case, the genes are labelled I, O, and P. The I, O, and P controller genes work very differently from the A, B, and C genes that the subjects had just learned. Here, the I and O genes inhibit the activity of the enzyme producing genes until a nutrient is present (as in Figure 1). Note that in the training phase subjects learned that gene regulation can occur by activation (one gene switches other genes on), but that in the second part of the study the type of genetic regulation to be discovered is very different, the subjects must discover inhibition (genes turn other genes off).

There are 120 possible experiments that can be conducted. Different types of experiments produce different amounts of enzyme given a certain amount of nutrient. For an experiment with normal Ecoli, the amount of enzyme produced is half whatever the amount of nutrient is. Mutants with the I gene missing (designated I- mutants) produce an output of 876, and O- mutants produce an output of 527. The I- and O- mutants produce this amount of enzyme regardless of the amount of nutrient administered. Thus, I- and O- nutrients will produce enzymes even when no nutrient is administered. This is a strong clue for inhibition being involved. In Study 1, the P gene plays no role at all. A mutant with a P gene missing (P-) will produce the same amount of nutrient as the normal ecoli. That is, the P gene plays no role in Study 1. In the real ecoli, and in Study 2, the P gene does play a role.

The to-be-discovered mechanism is very different from the mechanism that subjects learned during training. The mechanism learned during training was activation -- the controller genes turn the enzyme producing genes on. The to-be-discovered mechanism is inhibition -- the controller genes inhibit the enzyme producing genes. It was expected that subjects initial hypotheses would be that the controller genes turn the enzyme producing genes on. Because the genes work by inhibition, subjects initial hypotheses will be disconfirmed and they will have to do a considerable amount of experimentation and hypothesis generation before they discover that the mechanism of genetic control is inhibition.

Research questions. The first set of questions focus on subjects use of disconfirming evidence. It was expected that subjects initial hypotheses would be that either the I, P, or O genes turn on the enzyme producing genes. These initial hypotheses would be disconfirmed after a few experiments. A number of possible strategies could be used at this point. One strategy would be to ignore the disconfirming evidence. This is a common finding when subjects cannot think of alternate hypotheses (cf. Einhorn & Hogarth, 1987; Klahr & Dunbar, 1988). Another strategy would be to use disconfirming evidence to modify the current hypothesis, but stay within the current frame. In this experiment, it would entail switching from one activation hypothesis to another. Again this is an approach that has been mentioned but not well documented (cf. Klahr & Dunbar, 1988). Another strategy would be to focus on the disconfirming evidence and attempt to discover what the cause of the surprising findings is. Many theorists have argued that this is a useful strategy, but there has been little evidence for the use of this strategy (e.g., Kulkarni & Simon, 1988; Einhorn & Hogarth, 1982).

A second set of questions are concerned with the processes that govern the generation of hypotheses and experiments. Klahr and Dunbar (1988) have proposed that scientific reasoning can be described as a search in an Hypothesis and an Experiment space. We identified a number of different strategies for searching both spaces: some subjects mainly searched the hypothesis space, and others switched to searching an experiment space. In the genetics domain, the hypotheses are more complex, and no single result provides enough evidence to confirm an hypothesis. Would the search strategies be similar in a radically different domain?

STUDY 1: DISCOVERING THE MECHANISM OF GENETIC CONTROL

Method

Subjects. Twenty McGill undergraduates were paid to participate in a 2 hour study. All subjects had taken one introductory biology course and none of the subjects knew about gene

regulation. Their knowledge of molecular genetics consisted of knowing that DNA and RNA exist and having a vague idea of how this is involved in gene reproduction.

Procedure. The study was carried out in three phases. First, the subjects were taught some basic facts about molecular biology, and were shown how a gene could be switched on by another gene. Second, the subjects were instructed on how to give a verbal protocol (cf. Ericsson & Simon, 1984). The subjects were given a 15 puzzle and were asked to think out loud while they solved the puzzle. Third, subjects were shown a new set of genes that produce a beta enzyme when there is lactose present and no beta enzyme when lactose is not present. They were told that the I, P, and O genes were potential candidates for controlling the beta genes and that their task was to discover how the beta genes are controlled. The subjects were told to state everything that they were thinking while they were performing the task. Subjects were told that they could finish either when they felt that they had discovered how the beta genes were controlled, or when they felt that they could not discover how the beta genes are controlled. If the subjects had not discovered how the genes are controlled within ninety minutes the study was stopped.

RESULTS

Two criteria for success were adopted in analyzing the results of this study. The first criterion was that subjects who determined that the I and O genes inhibit the production of beta were successful. Five subjects were able to determine that the mechanism of gene control was inhibition. The second criterion was that subjects who discovered that the O gene had to be on the same gene as the beta genes, and postulated a mechanism that could account for these findings. Two of the five subjects reached this criterion. Subjects took, on average, 60 minutes to do the task. There was no significant difference in the amount of time it took the subjects who succeeded (criterion 1) and those who did not. Subjects conducted an average of 16 experiments. There was no significant difference in the number of experiments by those who succeeded and those who did not. Of the 16 experiments, 13 were conducted with greater than zero amounts of lactose, and 3 were conducted with zero lactose.

The results of the study will be analyzed in terms of the strategies that subjects used after obtaining disconfirming evidence for their initial hypothesis. As expected, all subjects initially proposed that either the I, O, or P genes, or a combination of these genes turns on the enzyme producing genes. Eighteen of the twenty subjects tried a P-, O-, I- mutants with the same amount of lactose for their first three experiments. Subjects set their initial goal to find the activator gene. To achieve this goal they attempted to discover a situation that when the gene was absent the ecoli would not produce any enzyme. However, this initial goal was not fulfilled. Subjects did not find a situation where there was no output with a gene missing. The subjects discovered that when the I or O genes were missing there was a large output of enzyme, and that when the P gene was missing the ecoli behaved normally.

At this point, subjects adopted three different strategies for dealing with disconfirmation. One group stayed within their Activation frame and distorted the logic of experimentation to maintain their hypothesis. A second group embarked upon a search for a particular experimental result that would demonstrate activation. A third group switched their goal from one of finding activation to attempting to discover the cause of the unexpected findings. These strategies will now be discussed in detail.

Strategy A: Maintain frame By changing Logic of interpretation (N=6). Once these subjects obtained evidence that did not fit in with their initial hypothesis, they maintained the goal of finding an activator gene. However, they changed the logic of evidence interpretation. Their original goal was to discover that when a particular controller gene was missing no enzyme would be produced. Much to their surprise, they discovered that, no matter what gene was missing, there was always an output of enzyme. They also discovered that some mutants resulted in less output than others. They then proposed that if the controller gene is absent then there is little output. They substituted little output for no output. They argued that the gene that is absent when the least output appears is the controller gene. The P gene -- which has no role whatsoever -- is absent when the least output appears and this group of subjects argued that the P gene is the controller gene. As a way of testing this hypothesis they proposed that if the P gene is present

there will be a large output. Using this strategy, these subjects noticed that mutations with the P gene present produce large amounts of enzyme and concluded that the P gene is the controller gene.

It is important to note that the P gene plays no role whatsoever in controlling the genes. The subjects notice that when P is present the most enzyme is produced, and that when it is absent the least amount of enzyme is produced. They conclude that P activates the *E. coli* to produce a certain amount of enzyme. To reach this conclusion, subjects must ignore the fact that a normal gene only produces small amounts of enzyme and the P gene is present. Also, there are 4 diploid experiments that disprove this hypothesis and all the subjects in this group conducted at least one of these experiments. Subjects in this group all had a constrained search of the experiment space. The subjects did not conduct experiments with zero amounts of lactose. This is because their goal was to discover activation, therefore a zero lactose experiment was regarded as unnecessary.

In summary, the strategy that this group used was one of setting up a goal of discovering an activator gene. All subjects stated that this was their goal. When this goal was not fulfilled, the subjects distorted the logic of evidence interpretation until their goal of discovering the activator gene was fulfilled. The goal of finding activation constrained every stage of the discovery process.

Strategy B: Search Experiment Space (N=7). At the end of the first phase these subjects proposed that the mechanism probably involves some interaction of the genes and they hoped to find a certain combination of mutant genes that will not produce an enzyme when there is lactose present. To achieve the goal of finding this result they parametrically searched for an experiment that would produce this result. These subjects conducted more experiments and also searched different regions of the experiment space. However, they eventually gave up because they could not find an experimental result that fills the goal of discovering an activator gene.

Strategy C: Opportunistic Subgoal (N=7). This group initially believed that the controller gene works by activation, however as with the other two groups, they discovered that no matter what type of mutation there was always an output. However, instead of maintaining the goal of finding a gene that will not produce an enzyme when there is lactose present, these subjects set a goal of discovering why such unexpected results occurred. They focused on why there is a large output for I and O mutants, why the output is instantaneous for I- and O- mutants, and why the amount of nutrient administered is irrelevant. They first proposed that the I and O genes control the size of the output. Then, when they realized that the amount is irrelevant, they conducted experiments with zero lactose, and proposed that the I and O genes work by inhibition. Five of the seven subjects in this group discovered inhibition. The other two subjects did not get past the stage of proposing that the I and O genes govern the amount secreted. In sum, this group of subjects made significant progress by setting up new goals rather than maintaining the original goal.

DISCUSSION

The results of this study suggest that the major effect of disconfirmation is to induce subjects to propose minor changes in hypotheses. Despite disconfirmation, subjects maintain their original frame and continue to search for a particular type of experimental result. Maintaining the goal can lead subjects to change the logic of data interpretation to fit in with the current hypothesis. Thus, it appears that the major difficulty that subjects have is of changing their goal from trying to generate a particular finding to one of trying to discover the cause of their unusual findings. The successful subjects abandoned the goal of discovering activation and set up a new goal of trying to account for the set of findings that they obtained. Thus the goal of finding a particular mechanism prevents subjects from discovering alternative mechanisms of genetic control.

If the goal of discovering activation prevents subjects from considering the nature of disconfirming evidence, and constrains search of both the Hypothesis and Experiment spaces, then if this goal is eliminated, the subjects should set a new goal and discover the correct solution. The second study was conducted to test this hypothesis.

STUDY 2: GOALS AND DISCOVERY

The results of Study 1 suggest that the goal of finding supporting evidence for the current hypothesis constrains search of the hypothesis and experiment spaces. To test this idea, the genetic mechanism was changed so that one gene works by activation-- the P gene. The I and the O genes still work by inhibition. The only change from study 1 is that the P gene must be present for the *E. coli* to secrete an enzyme. If the P gene is absent no enzyme is produced. The subjects now have to discover that the I and O genes work by inhibition, and that the P gene works by activation. Thus, the genes work in a more complex mechanism than in Study 1. One possible outcome of this manipulation would be that once the subjects have discovered the P gene works by activation they will say that they have discovered the genetic mechanism: They have achieved their goal and the task is done. Another possible outcome is that once the subjects have discovered activation, this goal will be popped and a new goal will be set of accounting for the other findings. If this occurs, then many more subjects should discover that the genes work by inhibition than in the Study 1. This finding would suggest that the goals of the subject constrain the scientific discovery process.

Method

Subjects. Twenty subjects participated in the experiment. The subjects were from the same population as those in Study 1.

Procedure. The procedure was identical to that used in Study 1: There were three phases, training, giving protocols, and discovering the mechanism of genetic control. The only difference between this and study 1 was that here the P gene was an activator gene: the P gene must be present for an output to occur.

RESULTS

Subjects took considerably less time than in Study 1. Subjects spent an average of 38 minutes on the task (Study 1: 60 minutes). The mean number of experiments conducted was 15 (Study 1: 16 experiments). Nineteen of the 20 subjects discovered that the P gene was an activator gene. Fourteen subjects discovered that the I and O genes work by inhibition (Study 1: 5 subjects). Eleven of the 14 subjects discovered activation before inhibition.

The results of this second study are consistent with the view that the current goal has a large effect on the hypotheses proposed and experiments conducted. When the top level goal of finding an activator gene is achieved, the subjects set themselves a new goal of discovering the cause of the other surprising results. Thus, many more subjects discovered inhibition in Study 2.

GENERAL DISCUSSION

Subjects do make use of disconfirming evidence. They use disconfirmation to generate new hypotheses and experiments. Disconfirming evidence is used to guide search through both the hypothesis and experiment spaces. However, Studies 1 and 2 demonstrate that there are some serious constraints on the search initiated after disconfirmation. The search is constrained by the current goal. The goal can be to find evidence in favor of the current hypothesis, or it can be to explain surprising results. If the goal is to find evidence in favor of the current hypothesis, the goal can have major effects on the reasoning strategies used: Subjects consider few alternate hypotheses, and they distort their analyses of experimental results. This result suggests that some of the findings of faulty uses of logic (e.g., Wason's 2 4 6 task) is due to the goal that the subjects have rather than an inability to reason in a normative manner.

Subjects propose an hypothesis and set up an experimental goal. They then search the experiment space to achieve the goal. When the goal is not achieved they continue to search the Experiment space. Rather than popping back up to the Hypothesis space to formulate new hypotheses, subjects stay at an experimental level. The strategy that they use to formulate new hypotheses depends on setting a new experimental goal: accounting for the unexpected findings. This new goal allows them to generate evidence over which new hypotheses can be induced. It is only then that subjects pop back to the Hypothesis space and propose radically new hypotheses. This suggests that the problem for subjects is not that they are always looking for evidence that confirms their current hypothesis, but that they are engaged in Experiment space search trying to

achieve a certain experimental result. Subjects either have to change their experimental goal (as in study 1), or reach their goal before they can consider new hypotheses (as in study2). Thus, it is the goal that subjects have that is the source of confirmation bias, rather than the hypothesis per se.

While the negative side of goals constraining search is apparent, there are also a number of computational advantages to constrained search. In fact, many AI programs constrain search by the current goal (e.g., Turner, 1988). By using the current goal to constrain search, subjects only have to consider a small number of hypotheses, and also conduct a small number of experiments. Thus, the current goal prunes both the hypothesis and experiment spaces, making the problem tractable. Thus, the strategies discovered here may be in general useful, but because of their conservative nature, make it difficult to overthrow current theories.

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