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Procedural knowledge in molecular biology

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ABSTRACT *A crucial part of the knowledge of molecular biologists is procedural knowledge, that is, knowledge of how to do things in laboratories. Procedural knowledge of molecular biologists involves both perceptual-motor skills and cognitive skills. We discuss such skills required in performing the most commonly used molecular biology techniques, namely, Polymerase Chain Reaction and gel electrophoresis. We argue that procedural knowledge involved in performing these techniques is more than just knowing their protocols. Creative exploration and experience are essential for the acquisition of procedural knowledge in molecular biology. With enough experience, molecular biologists make intuitive judgments without recourse to analytical reasoning. We propose that procedural knowledge is intuitive recognition of the patterns of one's environment that are the most relevant for making a decision or acting appropriately. Finally, we argue that knowledge of molecular biologists requires an integration of procedural knowledge and propositional knowledge.*

1. Introduction

Scientific knowledge in molecular biology and other fields consists of at least three kinds of information—observation, laws, and theories: observations are generalized into laws, which in turn, are explained by theories. However, the day-to-day practice of molecular biologists reveals that much goes on before they can get even close to scientific observations. According to one estimate, molecular biologists "spend about 99% of … [their] time tinkering with protocols and genes and such, and only a tiny bit of time—probably less than an hour a week—actually thinking about the implications, or theory, or whatever of it all" (Shrager, 2000). They must get their hands dirty with myriad physical objects, organic and inorganic, while using laboratory apparatus to carry out many procedures that provide data for models of biological processes.

We argue in this paper that a crucial part of the knowledge of molecular biologists is procedural knowledge, which is knowledge of *how* to do things. Pro-

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cedural knowledge is contrasted with propositional knowledge, which is knowledge *that* something is the case. Our goal is to show that what molecular biologists know is not just knowledge of facts about cellular molecules or theories that explain the workings of those molecules, but also knowledge of ways of doing things in their laboratories.

We build our case by presenting information from two primary sources. The first is *Diary of an insane cell mechanic*, by Jeff Shrager (2000). This online diary is a fascinating and lucid log of experiences of a molecular biologist in the making. Shrager earned a PhD in cognitive psychology and has worked as a research scientist in diverse areas, including neuroscience and computational drug discovery. The second source is Steve Kales, a graduate student of molecular biology at the University of Waterloo, whom we interviewed and also observed while he performed the common techniques in his laboratory (Kales, 2001). We discuss specific examples of the procedural knowledge employed in using the techniques of Polymerase Chain Reaction (PCR) and gel electrophoresis. We argue that the versatility and ubiquity of these techniques allows us to generalize our claims. We propose that procedural knowledge involves intuitively recognizing patterns of the features of the scientist's situation that are the most relevant to making the decision or performing the task at hand. We conjecture that procedural knowledge in molecular biology is acquired by constructivist learning proposed by Quartz and Sejnowski (1997, 2002) in their theory of neural constructivism. We conclude with a discussion of the complex interplay of knowledge-that and knowledge-how in the everyday practice of molecular biologists.

2. Procedural knowledge vs. propositional knowledge

Ryle (1949) introduced the contrast between "knowing how" and "knowing that" with knowledge-how thought of as an ability to do something. In psychology, the terms "explicit knowledge" and "implicit knowledge" are commonly used for propositional and procedural knowledge, respectively; explicit refers to conscious knowledge and implicit to unconscious knowledge (Reber, 1989). Sometimes, procedural knowledge is seen as knowledge of skills (Yamadori *et al.*, 1996). In artificial intelligence, the term "declarative knowledge" is often used for knowledge of facts, which is contrasted with procedural knowledge (Sun *et al.*, 2001). In psychology and AI, researchers use the terms, "explicit knowledge" and "declarative knowledge" interchangeably. Similarly, although "implicit knowledge" is the most commonly used term in psychology for knowledge-how, psychologists also use the term procedural knowledge. The different terms used in relation of knowledge-that and knowledge-how in the respective disciplines are listed in Table 1.

Procedural knowledge often involves technological skills, but people employ a wide range of procedural skills. "Design modeling, problem solving, system approaches, project planning, quality assurance and optimization" are various kinds of technological procedural knowledge (McCormick, 1997, p. 144). The most widely studied skill knowledge in AI is "cognitive skill acquisition" (van Lehn, 1995) which refers to learning to solve problems in domains, such as arithmetic puzzle solving,

TABLE 1. Different terms used with respect to knowledge-how and knowledge-that

Philosophy	Knowledge-that, propositional knowledge	Knowledge-how, procedural knowledge, abilities
Psychology	Explicit knowledge, declarative knowledge	Implicit knowledge, tacit abilities, skills
Artificial intelligence	Declarative knowledge	Procedural knowledge

elementary geometry and LISP programming (Anderson, 1982; Rosenbloom *et al.*, 1993; van Lehn, 1990, 1995).

Neuroscientists typically study low-level skills such as the ones needed for verbal production tasks and maze tasks (Petersen *et al.*, 1998), mirror reading and mental rotation (Timmerman & Brouwer, 1999; Yamadori *et al.*, 1996), serial reaction time tasks (Pascual-Leone *et al.*, 1999), and Braille-reading by the blind (Hamilton & Pascual-Leone, 1998). Psychologists have studied procedural knowledge in tasks such as dynamic control tasks (Berry & Broadbent, 1988), artificial grammar learning tasks (Reber, 1989), and serial reaction tasks (Willingham *et al.*, 1989). Thus, procedural knowledge varies in complexity and degree of cognitive involvement, from simple motor skills to highly intellectual skills.

In contrast to the widely accepted distinction of procedural and propositional knowledge, Stanley and Williamson (2001) have recently argued that procedural knowledge is a species of propositional knowledge. Their argument consists of two parts: a syntactic analysis and a semantic analysis of ascriptions of knowledge-how and ascriptions of knowledge-that. Relying on recent syntactic theory, Stanley and Williamson show that the supposed linguistic distinction between ascriptions of knowledge-how, sentences such as (1) below, and ascriptions of knowledge-that, sentences such as (2) below, has no basis in the structure of the two sentences:

(1) Hannah knows how to ride a bicycle, and
(2) Hannah knows that penguins waddle.

In the view of Bechtel and Abrahamsen (1991) that Stanley and Williamson discuss, in sentences such as (1), "knows how" forms a constituent with no clausal complement. The expression "to ride a bicycle," which is a description of an action, is the complement of the "know how" constituent. In (2), "that penguins waddle" is the clausal complement of "knows." Using recent syntactic theory, Stanley and Williamson show that there are only two syntactic features of sentences like (1) that distinguish them from sentences such as (2). First, (1) contains embedded questions whereas (2) does not; and second, (1) contains an untensed clause whereas (2) contains a tensed clause. (They show that there is no conceptual connection between these two syntactic features.)

Stanley and Williamson argue that it is incorrect to say that "knows how" is a constituent in sentences such as (1), since embedded "how" questions with untensed clauses are not restricted to co-occurring with "know"; they can co-occur with other kinds of verbs as in sentences (3a)–(3f):

(3a) Hannah learned how to ride a bicycle,
(3b) Hannah recalled how to ride a bicycle,
(3c) Hannah asked how to ride a bicycle,
(3d) Hannah wonders how to ride a bicycle,
(3e) Hannah is certain about how to ride a bicycle, and
(3f) Hannah indicated how to ride a bicycle.

According to Stanley and Williamson, the correct constituent structure of sentence (1), an ascription of knowledge-how with an untensed clause, is as follows:

(4) Hannah knows [how PRO to ride a bicycle t].

"PRO" in sentences like (4) is a phonologically null pronoun that occurs in the subject position of untensed clauses. The occurrence of "t" indicates the trace of the movement of "how" from the site where "t" occurs. Now consider an embedded question with a *tensed* clause that clearly attributes propositional knowledge to the subject:

(5) Hannah knows how Bill rides a bicycle.

Stanley and Williamson argue that from the point of view of syntactic theory, there is no difference between (1) and (5) that would lead us to believe that (1) ascribes non-propositional knowledge whereas (5) ascribes propositional knowledge. The only syntactic difference between (1) and (5) is that (1) contains a phonologically null pronoun, indicated by "PRO" in (4), whereas (5) contains an overt noun "Bill." Thus, considering the correct syntax of constructions such as (1), we have no basis to claim that (1) ascribes non-propositional knowledge to Hannah.

Stanley and Williamson then turn to the standardly accepted semantics to analyze sentences like (1). They show that there are two complications involved in the interpretation of embedded questions with untensed clauses. First, the occurrence of "PRO" in such sentences have two interpretive possibilities; one being "PRO" receiving its interpretation from the subject of the main clause, and the second being "PRO" meaning something like "one." (This will become clear via an example shortly.) The other complication is that an infinitive in constructions like (1) also has two relevant interpretations; one being the infinitive having "ought"-like force, and the second being the infinitive having "can"-like force. Now consider the sentence (6) that is the same as (1) with "PRO" added at the appropriate place:

(6) Hannah knows how PRO to ride a bicycle.

There are four interpretative possibilities of this sentence:

(7a) Hannah knows how she ought to ride a bicycle,
(7b) Hannah knows how one ought to ride a bicycle,
(7c) Hannah knows how she could ride a bicycle, and
(7d) Hannah knows how one could ride a bicycle.

According to Stanley and Williamson (2001, p. 425), (7a) and (7b) "quite obviously" attribute propositional knowledge to Hannah. They think that interpretations

of (7c) and (7d) seem to be at issue in discussions of knowledge-how, focusing their discussion on (7c) which they think is "the paradigm reading" of (6).

Stanley and Williamson (2001, p. 425) claim that, according to the standard semantics, (6) (read as (7c)) is true "if and only if Hannah knows some proposition of the relevant form; that is, for some way w, Hannah knows that w is the way for Hannah to ride a bicycle." They add that this is not a semantic difference between constructions like (6) and other sentences involving other kinds of embedded questions. In general, sentences involving embedded questions are ambiguous between the "mention-all" and "mention-some" readings. Although, embedded questions involving "know how" often favor the "mention-some" reading, they are nevertheless ambiguous between these two readings. The fact that (6) favors "mention-some" reading is due to the "distinctive communicative purpose of the relevant class of uses" of this sentence (2001, p. 426). In other sentences such as (8 a–b), it is "natural" to favor "mention-all" reading (2001, p. 426).

(8a) The warden of the prison knows how to escape from it.
(8b) The expert pitching coach knows how to pitch to a dangerous switch-hitter.

Therefore, relative to the context in which (6) is interpreted as (7c), (8) is true if and only if "for some contextually relevant way w which is a way for Hannah to ride a bicycle, Hannah knows that w is a way for her to ride a bicycle" (2001, p. 426). Thus, according to Stanley and Williamson, if the standard account of the syntax and semantics of embedded questions are correct, then to say that someone knows how to F is always to ascribe to them knowledge-that. In short, according to them, knowledge-how is a species of knowledge-that.

We think that a purely linguistic analysis is inadequate to differentiate procedural and propositional knowledge. After presenting our study of procedural knowledge in molecular biology, we will return to Stanley and Williamson's view that procedural knowledge is a variety of propositional knowledge, and we will argue that their claim is untenable.

3. Procedural knowledge vs. knowledge of protocols

To avoid confusion, we begin by distinguishing "protocols" and "procedures." In biology, a protocol is a plan with specific instructions for steps to be followed to conduct an experiment. The word "procedure," however, is used in at least two ways. First, a procedure is a general way of performing or effecting something; this is the meaning behind our discussions of procedural knowledge. The term "procedure," however, is also commonly used to describe a specific series of steps taken to accomplish an end, such as the biological procedure of gel electrophoresis, which we will discuss in detail later. A procedure in this sense is very close to a protocol: a series of steps to do something *is* a plan to do something.

In molecular biology, there are different levels of procedures (Shrager, 2000):

- One minute or less: e.g. spinning down a mixture
- Five minutes: e.g. setting up a single PCR

- Fifteen minutes: e.g. spinning down the steps in a DNA extraction
- Half an hour to one hour: e.g. an enzyme reaction
- Overnight: e.g. PCR amplification
- One to two days: e.g. growing up a usable liquid culture from a plate pick
- One to two weeks or more: e.g. growing colonies from single cells

Molecular biologists commonly describe all of the above as procedures.

However, procedural knowledge is not knowledge of protocols. Procedural knowledge is knowledge of ways of doing things, and it is usually quite difficult to fully capture ways of doing things using only propositions. Protocols are propositions describing steps to follow in a plan. Procedural knowledge is *not* knowledge of protocols, for some people might memorize all the steps of a protocol of a technique yet may not be able to use the technique themselves in a laboratory. There is a very good reason why undergraduate molecular biology courses have mandatory laboratory exercises. Getting textbook knowledge is not enough; students must know how to perform the procedures in real laboratory conditions. To avoid any confusion between procedures and protocols, we will use the term "technique" instead of "procedure" to describe gel electrophoresis and other techniques of molecular biology.

We next discuss two techniques of molecular biology, namely, Polymerase Chain Reaction (PCR) and gel electrophoresis. We will describe them in general terms and then present their protocols, followed by our descriptions of the knowledge-how involved in performing these techniques.

4. Polymerase Chain Reaction

4.1. The technique of PCR

PCR is a technique used to directly amplify DNA sequences beginning with a DNA sequence that needs to be either recovered from a mixture or amplified. The sequences of the ends of the DNA segment are known, and the DNA is digested into large fragments using a restriction enzyme that recognizes and cleaves a specific short sequence, the restriction site, in double-stranded DNA molecules. The digested DNA is then heated to separate into single strands. The DNA segments are amplified by multiple cycles of DNA synthesis from short primers. A primer is a short nucleic acid sequence containing a free 3' hydroxyl group that forms base pairs with a complementary template strand and functions as the starting point for addition of nucleotides to copy the template strand. The multiple cycles of DNA synthesis are followed by brief heat treatment to separate the complementary strands. At each round, the number of copies of the sequence between the primer sites is doubled. Thus, the instances of desired sequence increase exponentially (Lodish *et al.*, 2000, pp. 246–248).

A standard PCR protocol, such as the one by Bowtell (1995), includes specifications of the reagents to be used, descriptions of the various stages of the reaction, and a template of relative amounts of different reagents used in the reaction. The PCR machine cycles the temperature of the reaction mixture

repeatedly. The experimenter prepares the reaction mixture according to the specifications of a protocol, puts the reaction mixture into the PCR vessels, puts the PCR vessels into the machine, and the machine does the rest.

4.2. Procedural knowledge of PCR

There are many things that are not made explicit in the protocol, including specifications that depend on the type of the DNA being used. For example, the protocol does not explicitly tell which restriction enzyme to use or which primer to use, although the protocol could be made more specific. However, there are some things that *cannot* be made explicit in the protocols. Here is an example from Shrager (2000): *how* do the experimenters get the multiple 1–3 micro-liter droplets of liquid all into the bottom of the PCR vessel? The answer would be very obvious to molecular biologists: use the device called a pipette. But how do they use a pipette? They put the pipette body in a pipette tip, set the desired amount of liquid they need by rotating a knob and reading the counter in the middle of the pipette body. They press on the knob at the top of the pipette body, insert the knob into the liquid and release it to fill the tip with precisely the amount of the desired liquid. In order to deliver the liquid into a PCR vessel, they simply insert the pipette tip into the vessel and press on the knob and release it. Molecular biologists use PCR quite commonly, and they use pipettes even more frequently. So, they must know *how to* use a pipette in order to put micro-liters of liquid into the bottom of the PCR vessel.

Using a pipette is as easy for molecular biologists as using a spoon is for all of us, but when molecular biologists first learn how to use pipette, they can do several things wrong. They can fling the rack of pipette tips all over the place by putting the pipette body into it at the wrong angle without holding it at the same time. They can get the tip of the pipette caught on the rim of the vessel as they remove the pipette, and hence cause the vessel to bounce slightly and spill its contents all over the table (Shrager, 2000). In short, they could handle their equipment in any number of wrong *ways*.

In the above two paragraphs, we have used several sentences to describe how to transfer micro-liters quantities of a liquid into a PCR vessel, and we have described what can go wrong while doing so. We have described knowledge of a way of doing something in knowledge-that terms, and have added knowledge-that descriptions of a number of wrong ways of doing it. From reading our description of this knowledge-how and knowing the wrong ways of doing it, readers should not feel confident that they now have the knowledge of how to get micro-liters of liquid into the bottom of the PCR vessel. Even molecular biologists cannot tell that; the closest that they get to their knowledge-how is by using indexical terms, such as "*this* is how you do it" as they show how they do it by actually doing it. Procedural knowledge eludes propositional descriptions, but it remains a crucial part of the knowledge of molecular biologists.

In the next section, we will give another argument following the same reasoning we have followed in this section. We will give a general description of the technique of gel electrophoresis, and then describe specific steps of how it is done, and then

discuss the knowledge-how that cannot be made explicit in even the most specific instructions of how to perform it.

5. Gel electrophoresis

5.1. The technique of gel electrophoresis

Gel electrophoresis is a general term used to describe migration of bio-molecules towards electrical currents in a gel. It is a technique used for separating DNA or RNA or protein molecules according to their sizes or molecular weights. For instance, a cloned DNA fragment, released from its cloning vector—an agent that can carry DNA into a cell or organism—by digestion with the appropriate restriction enzyme, can be separated from the vector DNA by gel electrophoresis.

The technique consists of many subtasks, such as making the gel, loading the gel, and then running it. Here is a textbook description of instructions of how to perform gel electrophoresis, from Lodish *et al.* (2000, p. 229):

> A gel is prepared by pouring a liquid containing either melted agarose or unpolymerized acrylamide between two glass plates a few millimeters apart. As the agarose solidifies or the acrylamide polymerizes into polyacrylamide, a gel matrix … forms consisting of long, tangled chains of polymers. The dimensions of the interconnecting channels, or pores, depend on the concentration of the agrose or acrylamide used to form the gel. Because the pores are larger in agarose gels than in polyacrylamide gels, the former are used to separate large DNA fragments (from about 500 bp to about 20 kb) and the latter to separate small DNA fragments (1 nucleotide to about 2 kb). The mixture of DNA fragments to be separated is layered in a well at the top of the gel and an electric current is passed through the gel. DNA fragments move toward the positive pole at a rate inversely proportional to the log of their length, forming bands that can be visualized by autoradiography (if the fragments are radiolabeled) or by adding of a fluorescent dye such as ethidium. Agarose gels can be run in a horizontal orientation. … [T]he melted agarose is allowed to harden on a single horizontal glass or plastic plate. This is not easily done with polyacrylamide gels because oxygen in the atmosphere inhibits polymerization of acrylamide. Gels are generally depicted with the origin at the top and migration downward.

In simple terms, once a current is run along the gel, the different pieces of DNA move at different speeds along an electrical field from one end of the gelatinous surface to another. The viscosity of the gel slows the movement of the DNA pieces, impeding the smaller (the ones with smaller molecular weight) fragments less than the larger ones. So, the smaller pieces of DNA run faster. After about half an hour or so, DNA fragments are spread out along the gel from one another. To identify the DNA fragment of our interest, we can compare its size (in molecular weight) with

the different sizes of the DNA fragments on the DNA ladder, a standard series of bands of known sizes.

5.2. Procedural knowledge of gel electrophoresis

5.2.1. Perceptual-motor skills. The knowledge-how of gel electrophoresis is not apparent in the instructions of how to carry out the technique. Consider an example: how do you load the gel? You pipette it into the wells. Our discussion from the previous section regarding how to use a pipette is relevant here too. Furthermore, in order to get the liquid into the wells of the gel, molecular biologists have to be very good with their hands to do it in the right way. If their hands shake, the material floats to the surface instead of staying in the wells. Kales (2001) often had this problem when he learned to load gels in the beginning of his career, but he has gotten much better with practice. Shrager (2000) calls it "gel-loading weirdness" that was a recurring problem in the early stages of his learning.

Here is another "know-how" aspect of gel electrophoresis: once you have found the DNA of your interest, how do you get it out of the gel? Molecular biologists use a razor blade to cut out the slice of the gel that they think has the DNA of the desired size (Shrager, 2000). Again, they have to be good with their hands.

5.2.2. Cognitive skills. So far, we have argued that molecular biologists need perceptual-motor skills. But they also employ cognitive skills in interpreting gels. Using gel electrophoresis is "fuzzy" (Shrager, 2000). Kales (2001) agrees that it is hard to be precise with gels. Things (DNA or RNA or protein) do not really flow at perfectly even rates in every track on a gel. One must make judgments regarding issues, such as: "Is it a band or isn't it? Is it one band or two?" (Shrager, 2000) Sometimes the ladder (the size standard) gets all bunched up at the place where you want to read it, and the legend does not seem to match the ladder quite right. If this happens, how do you tell the sizes of the fragments? If two fragments are of the same size, they end up in the same place. How do you tell that one band has one or two fragments? "How do you interpret smearing? Is it important smearing? Should [you] ignore it, or change [your] levels of belief of the band amplitudes based upon the smearing?" (Shrager, 2000). As Shrager (2000) puts it, gel interpretation requires "flexibility or in-stream interpretation." As Kales (2001) puts it, "it is a skill." This is not to say that molecular biologists do not reason while interpreting gels. The crucial point is that most of the time they make judgments *before* they reflect. We will return to this point in Section 8, where we propose our formulation of procedural knowledge. So far, we have argued that molecular biologists employ both perceptual-motor and cognitive skills. In the next section, we will give another example of procedural knowledge in molecular biology.

6. "Playing around" is the mother of invention

We have been arguing that procedural knowledge is not knowledge of protocols. Learning procedural knowledge is also not a matter of mechanically following a

protocol. It is more like exploring different ways of doing things at different parts of the protocol. There is a remarkable similarity between Kales' description of this process, "playing around," and Shrager's descriptions, "monkeying around" and "tinkering with protocols." With experience, molecular biologists begin to take more liberties with protocols. This helps them to fine-tune protocols in ways that work best for them. More interestingly, exploration sometimes leads to new ways of doing traditional things. Molecular biology is a highly technical field. Often, the challenges that molecular biologists face are not theoretical or conceptual but technical; and sometimes the problems are solved by "playing around," that is, by creative explorations which enable molecular biologists to come up with modifications of previous ways of doing things.

Here is an example from Shrager (2000). For one of his experiments, the task was to get a small piece of *E. coli* (that had a gene of interest in it) off the agar plate on which Shrager had cultured it. How is it done? It is not advisable to simply scrape off the surface of the culture because no matter how careful you are, a chunk of agar gets scraped off along with the culture. So, the traditional way of doing it as follows. A 5-inch wire with a loop at the end is heated in a burner. The loop is dipped into the agar to cool it. Then, the loop is used to "saw" a square chunk of agar out of the plate by putting the loop into and pulling it out of the plate four times, once on each side of the square. The square of the chunk is then worried out with the wire loop. Shrager describes a problem with the last step: "Unless you have sawed it [the agar square] completely out, which is hard to do with a loop, it sticks to the rest of the plate, and then when you try to pull out the chunk, it won't come out cleanly, so you use more force, until … SPROING! it comes flying out and shoots across the room, or worse, contaminates something else on the plate or the hood" (Shrager, 2000).

To solve this problem, Shrager modified the traditional way of getting a small piece of *E. coli* off the agar plate. The first two steps of heating the loop and then cooling it in the agar remain the same. Shrager modified the subsequent steps as follows: "Plunge the loop into the plate next to the part you want to extract, then, instead of sawing out a block, just sort of move the handle in a circle in a certain way that slightly bends the wire. With a little practice this cuts an inverted cone (tip down) 'cleanly' out of the plate. Then all you need to do is get the loop under the tip of the cone and lift it out" (Shrager, 2000). It is a minor change but it made Shrager's technique a lot more efficient for him. Thus, exploration is an important part of acquisition of procedural knowledge in molecular biology. With enough experience, creative solutions to the technical problems of molecular biology just happen. In Section 8, we describe such intuitive experiences and argue that they are the hallmark of procedural knowledge, but first some words on how representative our claims are of the skills of molecular biologists.

7. Can we generalize?

One might question that our discussion is based on our study of skills involved in only two molecular biology techniques, namely, gel electrophoresis and PCR, and

that our sources of information are only two molecular biologists—namely, Shrager and Kales. In short, one might wonder if our claims are representative of the skills of molecular biologists in general.

We chose gel electrophoresis and PCR for our discussions because these are the most commonly used techniques in molecular biology labs. Kozulic (1995, p. 51) notes, "Gel electrophoresis is the most widely used method for the analysis of biological macromolecules, including proteins and nucleic acids." Gel electrophoresis of nucleic acids fits with many higher-level tasks, such as gene inactivation, restriction endonuclease reactions, purification by cutting out desired DNA fragments from the agarose gel, and DNA sequencing. Gel electrophoresis of proteins (e.g. 2D-PAGE or two-dimensional polyacrylamide gel electrophoresis) also has numerous applications, some of which are as follows: the analysis of phenotypic alterations in protein expression during both normal and abnormal growth and differentiation; the identification of specific protein changes induced by mutagens, carcinogens, hormone treatment, mitogen stimulation, nutrient changes; isoenzyme analysis for studying basic processes, such as the transformation of one gene into another, the regulation of gene expression, and the significance of metabolic pathways in different tissues; the characterization of human and animal tissues and cells; the isolation of extremely pure proteins for antibody production; and amino acid sequence analysis for subsequent applications, such as the synthesis of appropriate oligonucleotide probes for cDNA isolation, gene cloning, and subsequent genetic analysis (Meyers, 1995).

In recent years, PCR has become as ubiquitous as gel electrophoresis because PCR makes the information embedded in nucleotide sequences more accessible to molecular biologists. This technique is widely used for tasks, such as DNA sequencing, cloning DNA fragments, and site-directed mutagensis (Weiner *et al.*, 1995). Like gel electrophoresis, PCR is a versatile technique. Here are some of its applications: PCR facilitates oligonucleotide probe hybridization, and restriction site analysis; it allows the analysis of gene expression in specific cell lineages; it provides markers for genetic mapping; it facilitates the analysis of sequence variation for the identification of specific mutants; and it helps in generating the sequence database for phylogenetic analysis (Meyers, 1995). Meyers notes, "Several genome centers are designing major projects in which PCR plays a critical role in the screening of libraries or the development of high resolution physical maps prior to the actual sequencing steps" (1995, p. 53). Therefore, gel electrophoresis and PCR are excellent choices for our study of procedural knowledge in molecular biology because these techniques are versatile and ubiquitous.

Furthermore, PCR and gel electrophoresis are often used in conjunction with each other or with other techniques, depending on the research program of the molecular biologists. The following are a few examples. Molecular biologists working on DNA fingerprinting (for identification of unique profiles of different bacterial strains, for instance) employ both PCR and gel electrophoresis. Researchers working on proteins often use gel electrophoresis in combination with Western blotting and immunoblot analysis, using monoclonal and polyclonal antibodies for identification and analysis of individual proteins. Molecular biologists researching in genetic

mapping and ordering (e.g. the Human Genome Project) often use PCR in conjunction with FISH (Florescence In Situ Hybridization) and FACS (Fluorescence-Activated Chromosome Sorting). Molecular biologists involved in genetic linkage mapping (mapping of genetic traits in which distances are based on the measurements of the frequencies of coinheritance) analyze DNA polymorphism by employing techniques, such as Southern blotting followed by DNA hybridization, PCR and OLA (Oligonucleotide Ligation Assay). For molecular biologists working on genetic analysis of populations, PCR and gel electrophoresis are crucial techniques. Molecular biologists interested in genetic testing for mutations relevant for certain conditions (for basic research, clinical diagnosis, carrier detection or prenatal diagnosis) use PCR often in conjunction with Southern blotting and LCR (Ligase Chain Reaction). In short, different molecular biologists have different programs of research and they use different techniques in different combinations. However, whatever their line of research, molecular biologists almost invariably want to look at the presence, absence or relative amount of DNA or protein or RNA converted to cDNA (i.e. copy of a DNA) of a certain size, and to do so, they use gel electrophoresis. Often, the organic molecules they want to study are too small for even gel electrophoresis, and the tiny bio-molecules of their interest are often found in mixtures of many other molecules, organic and inorganic. In order to recover the bio-molecules of their interest or to amplify them, molecular biologists use PCR. Hence, the perceptual-motor skills and cognitive skills required in using the techniques of PCR and gel electrophoresis are quite general, and our discussion of such skills is representative of procedural knowledge of molecular biologists involved in many different research programs.

8. Procedural knowledge as intuitive recognition of patterns

So far, we have argued that knowledge in molecular biology is not only knowledge of facts and theories about bio-molecules, but also procedural knowledge of ways of doing things in laboratories. Decisions based on propositional knowledge are analyzable into the isolatable propositions that form the various parts of the reasoning behind the decisions. However, decisions that result from procedural knowledge are not subject to such an analysis. Such decisions are intuitive in that they are made quickly and effortlessly.

Intuition and emotions are interconnected, and they have a basis in biology. Damasio (1999) and his colleagues have found that certain brain-damaged patients lack an emotional reaction to anticipated consequences of good and bad decisions. In normal subjects, this intuitive system is activated long before they are consciously aware that they have made a decision. In a computational account, Thagard (2000) has proposed that intuitions reflect an overall assessment of what makes sense in a situation, and such an assessment involves emotional coherence. Thus, intuition and emotions are intertwined.

Many thinkers have tried to give intuition its due credit in expertise. Simon (1989) saw intuitions as judgments and decisions based on experience and skill. He saw the process of making these judgments as nonlogical. Logical processes involve

conscious thinking in which goals and alternatives are specified, as are the cost and/or benefits of the alternatives. Nonlogical processes, on the other hand, are subconscious; they "are only known by a judgment, decision, or action" (Simon, 1989, p. 24). Thus, the individuals, while making judgments intuitively, can give neither an account of the process of decision-making nor how they know it to be correct.

Molecular biologists make intuitive judgments quite frequently, and especially if they have gathered enough experience in building their expertise. In the later entries of his diary, Shrager (2000), using an analogy of playing a fugue, describes his experiences of practicing certain techniques as being in a "natural flow" with them or as "owning" them:

> When I'm playing a fugue, I usually don't play each part separately and interlace them, rather I just know the movements that I go through, and the themes come out right by virtue of Bach being a genius. I can "hear" each theme separately if I want to—in fact, I'm not sure that I can suppress them, and sometimes, though rarely, I can "reason" about them together … But rarely am I "playing" them as separate yet interlaced themes. What I'm usually playing is the whole piece as one unit. But there are those rare moments after hundred of passes at a particular piece, when I get a deep understanding of Bach. When I "am" Bach, so that, just for a few seconds, I am controlling the music, playing through it consciously as a set of specific themes that I know, can feel, and can control; can make parts faster or slower; can see the next note and choose it consciously (and sometimes wrongly!). At these moments I, not Bach, own the fugue … Am I getting to that point with some of these [molecular biology] protocols? I have so far run them rote from the book, being careful not to do anything even slightly wrong, and not make any changes in timing or amounts, but recently, I've advanced to "owning" some of [the molecular biology techniques], like gel running and digestion.

Shrager (2000) concludes his diary with another analogy:

> I've been noticing in my travels in [molecular biology] … points at which I don't have to think about things any longer to talk about them. This is the same sort of thing that happens when you learn someone's name. At first you have to think about what it is each time you want to refer to them, then there is a stage where, if you spend enough time with them, you don't have to think hard about it any longer, but it still doesn't really flow from you, and then there eventually comes a point where it does just flow. Your connection with that person is different in each of these stages, although I doubt that this has anything to do with the naming, but is analogous and correlated just in the sense that it happens in stages over time of familiarity. We don't have words for these stages: acquaintance, friends, and colleague don't register the right dimensions. First you have just met, then you work around them for a while, knowing who they are but unfamiliar with their

> habits in detail, and eventually they are part of the natural flow of your environment. The same, of course, is true with the tools of the trade [of molecular biology], both physical and conceptual.

It is clear from the above two excerpts from Shrager's diary that his experience with certain molecular biology techniques allows him to makes certain decisions with such fluidity that no thinking or effort is required.

Shrager is not alone in employing intuition in his work. Joseph Needham (1928, p. 36), a biologist who practiced in the 1920s, describes the paramount role of intuition in science:

> The fact that the scientific investigator works fifty percent of his time by non-rational means is, it seems, quite insufficiently recognized. There is without the least doubt an instinct for research, and often the most successful investigators of nature are quite unable to give an account of their reasons for doing such and such an experiment or for placing side by side two apparently unrelated facts. [A]nd not only by this partial replacement of reason by intuition does the work of science go on, but also to the … scientific worker … the structure of the method of research is as it were given, he cannot explain it to you, though he may be brought to agree *a posteriori* to a formal logical presentation of the way the method works.

Dino Moras, a molecular biologist, was asked to enlist the qualities of a successful researcher. His response was as follows: "You need luck, but also intuition and adaptability. A good scientist … follows the experiments, adapts as quickly as possible, and perseveres" (Moras, 2001). Hence, intuition is a significant part of the practice of molecular biologists.

Shrager does not use the word "intuition," but his descriptions fit Gary Klein's (1998) notion of intuition as recognition of key patterns without recourse to analytical reasoning. According to Klein (1998, p. 31), "intuition depends on the use of experience to recognize key patterns that indicate the dynamics of the situation." While recognizing things intuitively, we do not know how we do the recognizing. We are confronted with a situation, we size it up, and immediately know how to proceed. As Klein (1998, p. 33) puts it, "we are drawn to certain cues and not others because of our situation awareness." Klein's definition of intuition is similar to Dreyfus and Dreyfus's (1986) view of intuition as recognition of similarity without recourse to isolatable elements of the situation. Along the same lines, research by Norman and Brooks (1997) indicates that experts' ability of pattern recognition of the relevant features involves rapid and unconscious matching of the relevant pattern with a similar pattern in the warehouse of patterns that the experts have built through experience. In short, intuition involves pattern recognition.

We propose a formulation of procedural knowledge as intuitive recognition of the patterns of one's environment that are the most relevant for making a decision or acting appropriately. We make this claim by drawing on Klein's (1998) model of decision-making in naturalistic settings, the recognition-primed decision (RPD) model. According to the RPD model, if a pattern of features is typically encountered

when one faces the kinds of tasks that one currently faces, then it is recognized as the key pattern and certain expectancies, relevant cues, plausible goals, or appropriate actions follow from the recognition. If experts' expectancies are violated, as when they encounter an anomaly, they may try to clarify their interpretation of the situation by checking which interpretation best matches the features of the situation. In other words, they may try to modify their diagnosis of the key features of the environment. Alternatively, they may use the anomaly as an important piece of information to modify their experience of the situation itself. Once the key pattern is recognized and a decision to act in a particular manner is made, they may evaluate their decision or action by imagining how the course of action will play out. Klein calls it mental simulation. If the decision-makers anticipate difficulties in the course of action based on their mental simulation, they may revise the course of action, or may even reject it and look for other options; if no difficulties are anticipated, the action is implemented (Klein, 1998). Thus, often when experts deliberate, they do so *after* they have already intuitively made a decision.

In sum, decisions based on procedural knowledge are not analyzable into isolatable elements of a situation. Such decisions are intuitive in that they involve quick and effortless recognition of the key patterns of the situation. Procedural knowledge is intuitive recognition of the relevant patterns without recourse to analytical reasoning.

9. Tacit knowing and neural constructivism

Our account of procedural knowledge is similar to Michael Polanyi's theory of tacit knowing. Polanyi (1967, p. 4) asserts that in many domains we can know more than we can tell. For example, we can recognize thousands of faces, but we usually cannot tell how we recognize a face we know. Polanyi says that tacit knowing involves two terms such that we know the first term only by relying on our awareness of it for attending to the second. In our terminology, the first term is recognition of a pattern and the second term is an action or inference that is a response to the pattern. Greatly needed is a cognitive theory of procedural knowledge and tacit knowing that can answer the following questions. Why is it often so difficult to put procedural knowledge into words? Why does acquisition of procedural knowledge often require considerable sensory experience? Why are experts who have acquired much procedural knowledge able to recognize different situations and draw more inferences than novices?

Current computational theories of thinking have difficulty answering these questions. It might seem that the rule-based approach to cognition advocated by theorists such as Newell (1990) and Anderson (1993) could provide an account of procedural knowledge. On this view, expertise is taken as a set of rules of the form IF $<$pattern$>$ THEN $<$reaction$>$. However, this approach generally takes patterns in the IF parts of rules to consist of verbal clauses, so it cannot explain why procedural knowledge often depends on sensory experience and is hard to put into words. Holyoak (1991) argues for a connectionist account of expertise according to which decision-making is based on parallel constraint satisfaction. Aspects of a

situation are represented by neuron-like nodes that are connected by positive and negative constraints, and decision requires a process that computes how best to satisfy these constraints. Unlike sequential reasoning based on rules or logic, we have no conscious access to the parallel process of constraint satisfaction, so the connectionist approach explains why we often cannot tell how we recognize patterns. However, Holyoak's account does not explain how patterns such as the ones acquired by molecular biologists depend so heavily on sensory experience. There are neural network algorithms for learning from experience such as back propagation (Rumelhart & McClelland, 1986), which trains a neural network by changing connections between neurons based on errors that it makes. But most procedural knowledge is not acquired by supervised learning that corrects errors, but rather by the kind of exploratory activity that we discussed in Section 6.

The above limitations of currently prevailing cognitive models of expertise can be overcome by attending to features of a relatively new approach to computational neuroscience, neural constructivism (Quartz & Sejnowksi, 1997, 2002). On this view, cognitive development is a progressive increase in the structures underlying representational complexity, and this increase depends on interaction with a structured environment to guide development. Quartz and Sejnowski argue that learning in neural networks is not merely a matter of adjusting connection weights, but also involves forming of new dendrites that provide novel connections between neurons. These new connections make possible a kind of representational change that enables organisms to deal with novel and changing environments. Quartz and Sejnowski present evidence that dendrites actively seek out incoming activity and shape their responses to mirror that activity. They argue that intelligent behavior results, not from prewired modules or blank-slate learning, but from a prolonged period of development in which environmental structure shapes the brain activity that in turn builds the circuits underlying thought. Constructivist learning does not involve a search through a predefined hypothesis space, but rather the building of a hypothesis space by virtue of new representations forged from new dendritic connections. The construction of the learner's hypothesis space is sensitive to the problem domain facing the learner.

We conjecture that procedural knowledge in molecular biology is acquired by just the sort of constructivist learning proposed by Quartz and Sejnowski. Acquiring the ability to use a pipette or to interpret patterns in gel electrophoresis involves more than just learning rules or fine tuning existing neural connections. Rather, exposure to new visual patterns such as those presented by gel electrophoresis leads the brain to generate new kinds of representation that involve novel connections between neurons resulting from the formation of new dendrites. Neural constructivism explains why learning procedural knowledge usually requires repeated interactions with complex environments: it takes many trials to enable the brain to form the new connections that are needed to produce novel neuronal structures that are needed to represent previously unfamiliar patterns. Unlike verbal representations such as those that correspond to words, these neuronal representations are not accessible to consciousness, so people are often not aware of the patterns they are using or how they are using them. Hence neural constructivism can explain why

procedural knowledge is often tacit rather than explicit. The development of new kinds of representations explains the enhanced abilities of experts to recognize patterns in complex phenomena that are mysterious to novices. We have no direct evidence for a neural constructivist theory of procedural learning, but it seems to provide the best available approach to understanding how procedural knowledge develops. We conjecture that the dendritic growth that characterizes constructive learning involves not only new connections between neuronal groups that recognize perceptual features, but also connections with affective areas of the brain that associate such features with emotional valences.

10. Integration of procedural knowledge and propositional knowledge

Our discussion on procedural knowledge in molecular biology does not imply that molecular biologists lack propositional knowledge. They use propositional knowledge all the time. More importantly, however, knowledge of experts in molecular biology requires an *integration* of propositional knowledge and procedural knowledge.

Molecular biology is a "messy" science. Shrager (2000) describes the intricacy of molecular biology by distinguishing it from car mechanics:

> In car mechanics, the car has a few parts, and the parts are different enough from one another that you don't get them confused. Moreover, the car stays put (usually) when you stop working on it, and you can look it over, choose your next tool, unbolt something, set it aside, take a break for a week, and the state of the world as you left it tells you where you were. In molecular biology, there are a million (more!) almost-the-same pieces of material floating around invisibly. If you lose track of what you were doing, you can't just look at the state of things and tell where you were and what you have to do next. Even if you could SEE DNA, there'd be too much of it in too many possibly configurations to be able to figure out by looking at it where you were. So there's a huge cognitive load imposed upon the experimentalist to keep track of what's going on; what state things are left in, and where things are going. Moreover, unlike the car, DNA (and esp. living organisms) will take off and do whatever they do if you just leave them to themselves—hybridize or degenerate or overgrow or die. So not only do you have to know what is going on, you have to be able to make decisions on a schedule.

According to Shrager, molecular biologists have to keep track of what is going on while they are physically doing things; the practice of molecular biology is a complex interplay of molecular biologists' knowledge-that and knowledge-how.

"Playing around" or creative exploration helps molecular biologists in integrating their procedural knowledge and propositional knowledge. Apart from employing their perceptual-motor skills and cognitive skills, molecular biologists must also understand why a particular step is performed in a protocol. In other words, they have to use their knowledge-how in concert with their knowledge-that. Kales (2001)

explains that knowledge of why steps are used allows for creative exploration. For example, he modified nickel affinity chromatography to make it more efficient. He uses this technique to purify his desired recombinant protein from the mixture of host proteins (in *E. coli*). Kales (2001) describes his experience as follows: "I had no idea how to do it when I started, yet the protocol is quite specific, but with little explanations. As I determined what each step actually is used for, I started optimizing the … [technique] for my requirements. I now run two columns for two separate protein purifications at the same time." As another example, Kales uses ELISA (enzyme-linked immunosorbent assay) to test for antibody response from rabbits prior to injecting them with a particular protein. If the rabbits have antibodies that cross-react with the protein, then he would not be able to use them. Kales tailored his "made-up" protocol from four different protocols. He used different proteins in differing conditions and different antibodies than the four protocols specified. Procedural knowledge in molecular biology is not a matter of mindlessly following protocols. Molecular biology is about using the logic of the protocols, hence using the propositional knowledge of them, in concert with procedural knowledge, that is, perceptual-motor skills and cognitive skills. Most of the time, molecular biologists find the right harmony of their propositional and procedural knowledge by exploration.

The fact that molecular biologists are exploratory explains why things that work in a lab of one group of researchers may not work in a lab of another group (Kales, 2001; Shrager, 2000). As Kales (2001) puts it, "There are so many confounding variables in multi-step protocols that it is impossible to replicate all conditions during an experiment, especially when being performed by someone else in some other place." Different groups have different ways of using the same protocols, and labs are set up that way. A lot of times, researchers simply make minor changes in the specifications of the protocols depending on the type of equipment at their disposal; for example, they may skip steps that are not required for their needs or change incubation times or concentrations depending upon the equipment that is available (Kales, 2001). As a specific example, when Kales heat shocks competent *E. coli* cells for uptake of plasmid vectors, he uses a much longer heating time than is suggested in the protocol because that is what works best with the kinds of tubes at his disposal. If Kales were to use the exact specifications of the protocol, his cells would never take up the plasmid because they would not get heated enough. Nowhere does the protocol mention this, but Kales discovered it by playing around. His specifications would not work in another lab.

Exploration and experience go hand in hand. Apart from a sense of creative exploration, practice with techniques is an important part of training in molecular biology. Chronologically, molecular biologists first learn propositional knowledge of molecular biology techniques. For example, when they first try performing gel electrophoresis, they acquire knowledge-that of it—knowledge of what the technique is and what is the theory behind it, and knowledge about ways of doing it—from textbooks, and lab manuals. It is only with much practice, however, that they begin to "own" it; as Shrager (2000) explains, "The shape of gel purification is … three big 'lumps' (making the gel, running the gel, purifying the results), and each of these has

other lumps. The lumps have to be done in order but I know how to handle them—where I can pause, where I can't, how exact one needs to be with each. Moreover, at the same time that I was learning all of that, I was learning the physical skill of doing the unit tasks: taping the gels, pouring them, loading them, learning to 'see' the bands (with UV …), cutting out the bands, doing the purification procedure."

We contend that the sense of "owning" a technique comes after the integration of procedural knowledge of performing or doing it and propositional knowledge of the facts and theory behind the technique; and both exploration and practice are necessary for the integration. Shrager not only knows how to perform the different "lumps" of gel electrophoresis, he also has knowledge-that of it; for example, he has knowledge of "what it does, how it responds when … [he] flex[s] it, how to take it apart and interleave it with other procedures [techniques], and the way that it fits into other tasks" (Shrager, 2000). Therefore, through practice or experience, molecular biologists try to harmonize their knowledge-that and knowledge-how until procedural knowledge is fully acquired and intuitive judgments regarding the most relevant patterns of features of the situation are possible.

11. Dissociation of procedural knowledge and propositional knowledge

We hope that our paper has convinced the reader that Stanley and Williamson's (2001) position that procedural knowledge is a species of propositional knowledge is untenable. We have tried to show that knowledge of molecular biologists is not just propositional knowledge, but also procedural knowledge of how to do things in their laboratories. We are not alone in claiming that procedural knowledge and propositional knowledge are distinct. In this section, we briefly review the work of various researchers who have independently shown that explicit knowledge and skilled performance are distinct.

Researchers have demonstrated a dissociation of procedural knowledge and declarative knowledge in different kinds of tasks, such as dynamic control task (Berry & Broadbent, 1988), artificial grammar task (Reber, 1989), and serial reaction tasks (Willingham *et al.*, 1989). In these studies, subjects learned to perform the respective task without being given any *a priori* declarative knowledge and without being able to verbalize the rules they used to perform the task. In these examples, procedural knowledge is not correlated with declarative knowledge. Rabinowitz and Goldberg (1995) also show that there can be parallel learning at the declarative and procedural levels, separately. Furthermore, in some circumstances explicit knowledge may arise *from* procedural knowledge (Stanley *et al.*, 1989). Using a dynamic control task, Stanley *et al.* found that the development of declarative knowledge paralleled but lagged behind the development of procedural knowledge. Neuroscience studies on the famous patient H.M. also show dissociation of procedural knowledge and propositional knowledge. Due to a brain injury, H.M. lost his capacity to form explicit, declarative, long-term memories; he cannot retrieve sentences regarding his abilities. However, his abilities do improve, and he can learn new procedural knowledge (Cohen & Corkin, 1981; Cohen & Squire, 1980; Corkin,

1968; Milner, 1965). Therefore, procedural knowledge and propositional knowledge are clearly distinct from each other, and procedural knowledge is not a variety of propositional knowledge, as Stanley and Williamson (2001) hold.

12. Conclusion

We have argued that knowledge of molecular biologists is not just propositional knowledge of detailed models of what goes on in biological molecules, but also procedural knowledge of finding such details. Their knowledge-how consists of knowledge of ways of doing things that involve both perceptual-motor skills and cognitive skills. They employ their perceptual-motor skills in handling laboratory equipment, such as pipettes and test tubes. They use cognitive skills in tasks, such as interpreting gels. Their knowledge-how allows them to make intuitive judgments whereby they recognize patters of the most relevant features of their situation without recourse to isolatable elements of the situation. They acquire their procedural knowledge through neural constructivist learning. Knowledge of molecular biologists is a complex interplay of their knowledge-that and knowledge-how. We conclude with a quotation from Shrager's (2000) diary where he describes this complex interplay:

> It is these sorts of Knowing: Knowing what the protocols do, Knowing how to put them together to do larger tasks, Knowing how to make the whole thing work together smoothly, Knowing where you can start and stop and pause things, Knowing how to debug problems, Knowing what's going on all the time in all of your hundred variously labeled tubes in six different freezers at six different temperatures, Knowing the [DNA] sequences are of all your genes and how to manipulate them and reason about them, and Knowing in the end what the results mean in the larger conceptual space of biological science. It's these sorts of Knowing that make … [molecular biology] an interesting and difficult thing to do.

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References

ANDERSON, J.R. (1982). Acquisition of cognitive skill. *Psychological Review*, *89*, 369–406.

ANDERSON, J.R. (1993). *Rules of the mind*. Hillsdale, NJ: Erlbaum.

BECHTEL, W. & ABRAHAMSEN, A. (1991). *Connectionism and the mind*. Oxford: Blackwell.

BERRY, D. & BROADBENT, D. (1988). Interactive tasks and the implicit–explicit distinction. *British Journal of Psychology*, *79*, 251–272.

BOWTELL, D. (1995). *Bowtell lab manual*, v. 31.8.95; available online at: <http://grimwade.biochem.unimelb.edu.au/bowtell/molbiol/pcr.htm> (18 April 2002).

COHEN, N.J. & CORKIN, S. (1981). The amnestic patient H.M.: learning and retention of cognitive skills. *Society of Neuroscience Abstracts*, *7*, 517–518.

COHEN, N.J. & SQUIRE, L. (1980). Preserved learning and retention of pattern-analyzing skill in amnesia: dissociation of knowing how and knowing that. *Science*, *210*, 207–209.

CORKIN, S. (1968). Acquisition of motor skill after bilateral medial temporal lobe excision. *Neuropsychologia*, *6*, 255–265.

DAMASIO, A. (1999). *The feeling of what happens: body and emotion in the making of consciousness*. New York: Harcourt Brace.

DREYFUS, H.L. & DREYFUS, S.E. (1986). *Mind over machine*. New York: Free Press.

HAMILTON, R. & PASCAUL-LEONE, A. (1998). Cortical plasticity associated with Braille learning. *Trends in Cognitive Science*, *2*, 168–174.

HOLYOAK, K.J. (1991). Symbolic connectionism: toward a third-generation theories of expertise. In K.A. ERICSSON & J. SMITH (Eds) *Toward a general theory of expertise: prospects and limits* (pp. 301–335). Cambridge: Cambridge University Press.

KALES, S. (2001). Interview, by B. SAHDRA. University of Waterloo, Waterloo, 1 November.

KLEIN, G. (1998). *Sources of power: how people make decisions*. Cambridge, MA: MIT Press.

KOZULIC, B. (1995). Gel electrophoresis of DNA and proteins: recent advances in theory and practical applications. In A.M. GRIFFIN & H.G. GRIFFIN (Eds) *Molecular biology: current innovations and future trends*, *Part 1* (pp. 51–68). Norfolk: Horizon Scientific Press.

LODISH, H., BERK, A., ZIPURSKY, S.L., MATSUDAIRA, P., BALTIMORE, D. & DARNELL, J. (2000). *Molecular cell biology*. New York: W.H. Freeman.

MCCORMIC, R. (1997). Conceptual and procedural knowledge. *International Journal of Technology and Design Education*, *7*, 141–159.

MEYERS, R.A. (1995). *Molecular biology and biotechnology: a comprehensive desk reference*. New York: VCH Publishers.

MILNER, B. (1965). Memory disturbances after bilateral hippocampal lesions in man. In P.M. MILNER & S.E. GLICKMAN (Eds) *Cognitive processes and brain* (pp. 97–111). Princeton, NJ: van Nostrand.

MORAS, D. (2001). Interview, by L. SPINNEY. *HMS Beagle: The BioMedNet Magazine*, *111*, 28 September; available online at: <http://news.bmn.com/hmsbeagle> (18 April 2002).

NEEDHAM, J. (1928). Organicism in biology. *Journal of Philosophical Studies*, *3*, 29–40.

NEWELL, A. (1990). *Unified theories of cognition*. Cambridge, MA: Harvard University Press.

NORMAN, G.R. & BROOKS, L.R. (1997). The non-analytic basis of clinical reasoning. *Advances in Health Sciences Education*, *2*, 173–184.

PASCUAL-LEONE, A., TARAZONA, F., KEENAN, J., TORMOS, J.M., HAMILTON, R. & CATALA, M.D. (1999). Transcranial magnetic stimulation and neuroplasticity. *Neuropsychologia*, *37*, 207–217.

PETERSEN, S.E., VAN MIER, H., FIEZ, J.A. & RAICHLE, M.E. (1998). The effects of practice on the functional anatomy of task performance. *Proceedings of the National Academy of Science USA*, *95*, 853–860.

POLYANI, M. (1967). *The tacit dimension*. London: Routledge & Kegan Paul.

QUARTZ, S.R. & SEJNOWSKI, T.J. (1997). The neural basis of cognitive development: a constructivist manifesto. *Behavior and Brain Sciences*, *20*, 537–596.

QUARTZ, S.R. & SEJNOWSKI, T.J. (2002). *Liars, lovers, and heroes: what the new brain science reveals about how we become who we are*. New York: Morrow & William.

RABINOWITZ, M. & GOLDBERG, N. (1995). Evaluating the structure-process hypothesis. In F. WEINERT & W. SCHNEIDER (Eds) *Memory performance and competencies* (pp. 225–242). Hillsdale, NJ: Lawrence Erlbaum.

REBER, A. (1989). Implicit learning and tacit knowledge. *Journal of Experimental Psychology: General*, *118*, 219–235.

ROSENBLOOM, P., LAIRD, J.A. & NEWELL, A. (1993). *The SOAR papers: research on integrated intelligence*. Cambridge, MA: MIT Press.

RUMELHART, D.E. & MCCLELLAND, J.L. (1986). *Parallel distributed processing: explorations in the microstructure of cognition*. Cambridge, MA: MIT Press.

RYLE, G. (1949). *The concept of mind*. Chicago, IL: University of Chicago Press.

SHRAGER, J. (2000). *Diary of an insane cell mechanic*; available online at: <http://newatlantis.isle.org/~jshrager/diary/diary.html> (18 April 2002).

SIMON, H. (1989). Making management decisions: the role of intuition and emotion. In W.H. AGOR (Ed.) *Intuition in organization* (pp. 23–39). London: Sage.

STANLEY, J. & WILLIAMSON, T. (2001). Knowing how. *Journal of Philosophy*, *98*, 411–444.

STANLEY, W., MATHEWS, R., BUSS, R. & KOTLER-COPE, S. (1989). Insight without awareness: on the interaction of verbalization, instruction, and practice in a simulated process control task. *Quarterly Journal of Experimental Psychology*, *41A*, 553–577.

SUN, R., MERRILL, E. & PETERSON, T. (2001). From implicit skills to explicit knowledge: a bottom–up model of skill learning. *Cognitive Science*, *25*, 203–244.

THAGARD, P. (2000). *Coherence in thought and action*. Cambridge, MA: MIT Press.

TIMMERMAN, M.E. & BROUWER, W.H. (1999). Slow information processing after very severe closed head injury: impaired access to declarative knowledge and intact application and acquisition of procedural knowledge. *Neuropsychologia*, *37*, 467–478.

VAN LEHN, K. (1990). *Mind bugs: the origins of procedural misconceptions*. Cambridge, MA: MIT Press.

VAN LEHN, K. (1995). Cognitive skill acquisition. In J. SPENCE, J. DARLY & D. FOSS (Eds) *Annual review of psychology* (pp. 513–539). Palo Alto, CA: Annual Reviews.

WEINER, M.P., GACKSTETTER, T., COSTA, G.L., BAUER, J.C. & KRETZ, K.A. (1995). Recent advances in PCR methodology. In A.M. GRIFFIN & H.G. GRIFFIN (Eds) *Molecular biology: current innovations and future trends*, *Part 1* (pp. 11–24). Norfolk: Horizon Scientific Press.

WILLINGHAM, D.B., NISSEN, M.J. & BULLEMER, P. (1989). On the development of procedural knowledge. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *15*, 1047–1060.

YAMADORI, A., YOSHIDA, T., MORI, E. & YAMASHITA, H. (1996). Neurological basis of skill learning. *Cognitive Brain Research*, *5*, 49–54.