Introduction

"It is very difficult to find a black cat in a dark room," warns an old proverb. "Especially when there is no cat."

This strikes me as a particularly apt description of how science proceeds on a day-to-day basis. It is certainly more accurate than the more common metaphor of scientists patiently piecing together a giant puzzle. With a puzzle you see the manufacturer has guaranteed there is a solution.

I know that this view of the scientific process—feeling around in dark rooms, bumping into unidentifiable things, looking for barely perceptible phantoms—is contrary to that held by many people, especially by nonscientists. When most people think of science, I suspect they imagine the nearly 500-year-long systematic pursuit of knowledge that, over 14 or so generations, has uncovered more information about the universe and everything in it than all that was known in the first 5,000 years of recorded human history. They imagine a brotherhood tied together by its golden rule, *the Scientific Method*, an immutable set of precepts for devising experiments that churn out the cold, hard facts. And these solid facts form the edifice of science, an unbroken record of advances and insights embodied in our modern views and unprecedented standard of living. Science, with a capital *S*.

That's all very nice, but I'm afraid it's mostly a tale woven by newspaper reports, television documentaries, and high school lesson plans. Let me tell you my somewhat different perspective. It's not facts and rules. It's black cats in dark rooms. As the Princeton mathematician Andrew Wiles describes it: It's groping and probing and poking, and some bumbling and bungling, and then a switch is discovered, often by accident, and the light is lit, and everyone says, "Oh, wow, so that's how it looks," and then it's off into the next dark room, looking for the next mysterious black feline. If this all sounds depressing, perhaps some bleak Beckett-like scenario of existential endlessness, it's not. In fact, it's somehow exhilarating.

This contradiction between how science is pursued versus how it is perceived first became apparent to me in my dual role as head of a laboratory and Professor of Neuroscience at Columbia University. In the lab, pursuing questions in neuroscience with the graduate students and postdoctoral fellows, thinking up and doing experiments to test our ideas about how brains work, was exciting and challenging and, well, exhilarating. At the same time I spent a lot of time writing and organizing lectures about the brain for an undergraduate course that I was teaching. This was quite difficult given the amount of information available, and it also was an interesting challenge. But I have to admit it was not exhilarating. What was the difference?

The course I was, and am, teaching has the forbidding-sounding title "Cellular and Molecular Neuroscience." The students who take this course are very bright young people in their third or fourth year of University and are mostly declared biology majors. That is, these students are all going on to careers in medicine or biological research. The course consists of 25 hour-and-a-half lectures and uses a textbook with the lofty title *Principles of Neural Science*, edited by the eminent neuroscientists Eric Kandel and Tom Jessell (with the late Jimmy Schwartz). The textbook is 1,414 pages long and weighs in at a hefty 7.7 pounds, a little more in fact than twice the weight of a human brain. Now, textbook writers are in the business of providing more information for the buck than their competitors, so the books contain quite a lot of detail. Similarly, as a lecturer, you wish to sound authoritative, and you want your lectures to be "informative," so you tend to fill them with many facts hung loosely on a few big concepts. The result, however, was that by the end of the semester I began to sense that the students must have had the impression that pretty much everything is known in neuroscience. This couldn't be more wrong. I had, by teaching this course diligently, given these students the idea that science is an accumulation of facts. Also not true. When I sit down with colleagues over a beer at a meeting, we don't go over the facts, we don't talk about what's known; we talk about what we'd like to figure out, about what needs to be done. In a letter to her brother in 1894, upon having just received her *second* graduate degree, Marie Curie wrote: "One never notices what has been done; one can only see what remains to be done . . ."

This crucial element in science was being left out for the students. The undone part of science that gets us into the lab early and keeps us there late, the thing that "turns your crank," the very driving force of science, the exhilaration of the unknown, all this is missing from our classrooms. In short, we are failing to teach the *ignorance*, the most critical part of the whole operation.

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ONE
A Short View of Ignorance

Knowledge is a big subject. Ignorance is bigger. And it is more interesting.

Perhaps this sounds strange because we all seek knowledge and hope to avoid ignorance. We want to know how to do this, and get that, and succeed in various endeavors. We go to school for many years, in some cases now for more than 20 years of formal schooling, often followed by another 4–8 years of "on-the-job" training in internships, fellowships, residencies, and the like—all to gain more knowledge. But how many of us think about what comes after the knowledge is acquired? We may spend 20-plus years being educated, but what about the following 40 years? For those years we foolishly have no well-defined program, and much of the time we do not even have an inkling of what to do with them. So what does come *after* knowledge? You might not think of it in this order, but I would say that ignorance follows knowledge, not the other way around.

On her way into life-threatening surgery, Gertrude Stein was asked by her lifelong companion, Alice B. Toklas, "What is the answer?" Stein replied, "What is the question?" There are a few different versions of this story, but they all come to the same thing: Questions are more relevant than answers. Questions are bigger than answers. One good question can give rise to several layers of answers, can inspire decades-long searches for solutions, can generate whole new fields of inquiry, and can prompt changes in entrenched thinking. Answers, on the other hand, often end the process.

Are we too enthralled with the answers these days? Are we afraid of questions, especially those that linger too long? We seem to have come to a phase in civilization marked by a voracious appetite for knowledge, in which the growth of information is exponential and, perhaps more important, its availability easier and faster than ever. Google is the symbol, the insignia, the coat of arms of the modern world of information. More information is demanded, more facts are offered, more data are requested, and more is delivered more quickly. According to the Berkeley Institute, in the year 2002, 5 exabytes of information were added to the world's stores. That's a billion billion bits of data, enough to fill the Library of Congress 37,000 times over. This means 80 megabytes for every individual on the planet, equaling a stack of books 30 feet high for each of us to read. That was in 2002. It appears to have increased by a million times according to the latest update in this series for 2007.

What can one do in the face of this kind of information growth? How can anyone hope to keep up? How come we have not ground to a halt in the deepening swamp of information? Would you be suspicious if I told you it was just a matter of perspective? Working scientists don't get bogged down in the factual swamp because they don't care all that much for facts. It's not that they discount or ignore them, but rather that they don't see them as an end in themselves. They don't stop at the facts; they begin there, right beyond the facts, where the facts run out. Facts are selected, by a process that is a kind of controlled neglect, for the questions they create, for the ignorance they point to. What if we cultivated ignorance instead of fearing it, what if we controlled neglect instead of feeling guilty about it, what if we understood the power of *not* knowing in a world dominated by information? As the first philosopher, Socrates, said, "I know one thing, that I know nothing."

Scholars agree that Isaac Newton, in 1687, formulating the laws of force and inventing the calculus in his *Principia Mathematica*, probably knew all of the extant science at that time. A single human brain could know everything there was to know in science. Today this is clearly impossible. Although the modern high school student probably possesses more scientific information than Newton did at the end of the 17th century, the modern professional scientist knows a far, far smaller amount of the available knowledge or information at the beginning of the 21st century. Curiously, as our collective knowledge grows, our ignorance does not seem to shrink. Rather, we know an ever smaller amount of the total, and our individual ignorance, as a ratio of the knowledge base, grows. This ignorance is a kind of limit, and it's frankly a bit annoying, at least to me, because the one thing you know is that there is so much more out there that you will never know. Unfortunately, there seems to be nothing that can be done about this.

On the grander scale there is absolute or true ignorance, the ignorance represented by what really isn't known, by anybody, anywhere—that is, communal ignorance. And this ignorance, the still mysterious, is also increasing. In this case, however, that's the good news, because it's not a limit; it is an opportunity. A Google search on the word "ignorance" gives 37 million hits; one on "knowledge" returns 495 million. This reflects Google's utility but also its

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prejudice. Surely there is more ignorance than knowledge. And because of that there is more left to do.

I feel better about all that ignorance than I do about all that knowledge. The vast archives of knowledge seem impregnable, a mountain of facts that I could never hope to learn, let alone remember. Libraries are both awe inspiring and depressing. The cultural effort that they represent, to record over generations what we know and think about the world and ourselves, is unquestionably majestic; but the impossibility of reading even a small fraction of the books inside them can be personally dispiriting.

Nowhere is this dynamic more true than in science. Every 10–12 years there is an approximate doubling of the number of scientific articles. Now this is not entirely new—it's actually been going on since Newton—and scientists have been complaining about it for almost as long. Francis Bacon, the pre-Enlightenment father of the scientific method, complained in the 1600s of how the mass of accumulated knowledge had become unmanageable and unruly. It was perhaps the impetus for the Enlightenment fascination with classification and with encyclopedias, an attempt to at least alphabetize knowledge, if not actually contain it. And the process is exponential, so it gets "worser and worser," as they say, over time. That first doubling of information amounted to a few tens of new books or papers, while the most recent doubling saw more than 1,000,000 new publications. It's not just the rate of increase; it's the actual amount that makes the pile so daunting. How does anyone even get started being a scientist? And if it's intimidating to trained and experienced scientists, what could it be to the average citizen? No wonder science attracts only the most devoted. Is this the reason that science seems so inaccessible?

Well, it is difficult, and there is no denying that there are a lot of facts that you have to know to be a professional scientist. But clearly you can't know all of them, and knowing lots of them does not automatically make you a scientist, just a geek. There are a lot of facts to be known in order to be a professional anything —lawyer, doctor, engineer, accountant, teacher. But with science there is one important difference. The facts serve mainly to access the ignorance. As a scientist, you don't do something with what you know to defend someone, treat someone, or make someone a pile of money. You use those facts to frame a new question—to speculate about a new black cat. In other words, scientists don't concentrate on what they know, which is considerable but also miniscule, but rather on what they don't know. The one big fact is that science traffics in ignorance, cultivates it, and is driven by it. Mucking about in the unknown is an adventure; doing it for a living is something most scientists consider a privilege. One of the crucial ideas of this book is that ignorance of this sort need not be the province of scientists alone, although it must be admitted that the good ones are the world's experts in it. But they don't own it, and you can be ignorant, too. Want to be on the cutting edge? Well, it's all, or mostly, ignorance out there. Forget the answers, work on the questions.

In the early days of television, the pioneering performer Steve Allen introduced on his variety show a regular routine known as The Question Man. The world it seemed had an overabundance of answers but too few questions. In the postwar 1950s, with its emphasis on science and technology, it could easily have felt this way to many people. The Question Man would be given an answer, and it was his task to come up with the question. We need The Question Man again. We still have too many answers, or at least we put too much stock in answers. Too much emphasis on the answers and too little attention to the questions have produced a warped view of science. And this is a pity, because it is the questions that make science such a fun game.

But surely all those facts must be good for something. We pay a very high price for them, in both money and time, and one hopes they are worth it. Of course, science creates and uses facts; it would be foolish to pretend otherwise. And certainly to be a scientist you have to know these facts or some subset of them. But how does a scientist *use* facts beyond simply accumulating them? As raw material, not as finished product. In those facts is the next round of questions, improved questions with new unknowns. Mistaking the raw material for the product is a subtle error but one that can have surprisingly far-reaching consequences. Understanding this error and its ramifications, and setting it straight, is crucial to understanding science.

The poet John Keats hit upon an ideal state of mind for the literary psyche that he called Negative Capability—"that is when a man is capable of being in uncertainties, Mysteries, doubts without any irritable reaching after fact & reason." He considered Shakespeare to be the exemplar of this state of mind, allowing him to inhabit the thoughts and feelings of his characters because his imagination was not hindered by certainty, fact, and mundane reality (think Hamlet). This notion can be adapted to the scientist who really should always find himself or herself in this state of "uncertainty without irritability." Scientists do reach after fact and reason, but it is when they are most uncertain that the

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reaching is often most imaginative. Erwin Schrodinger, one of the great philosopher-scientists, says, "In an honest search for knowledge you quite often have to abide by ignorance for an indefinite period." (Schrodinger knew something about uncertainty; he posed the now famous Schrodinger's cat thought experiment in which a cat placed in a box with a vial of poison that could or could not be activated according to some quantum event was, until observed, both dead and alive, or neither.) Being a scientist requires having faith in uncertainty, finding pleasure in mystery, and learning to cultivate doubt. There is no surer way to screw up an experiment than to be certain of its outcome.

To summarize, my purpose in this intentionally short book is to describe how science progresses by the growth of ignorance, to disabuse you of the popular idea that science is entirely an accumulation of facts, to show how you can be part of the greatest adventure in the history of human civilization without slogging through dense texts and long lectures. You won't be a scientist at the end of it (unless you're already one), but you won't have to feel as if you're excluded from participating in the remarkable worldview that science offers, if you want to. I'm not proselytizing for science as the only legitimate way to understand the world; it's clearly not that. Many cultures have lived, and continue to live, quite happily without it. But in a scientifically sophisticated culture, such as ours, it is as potentially dangerous for the citizenry to be oblivious about science as it is for them to be ignorant of finance or law. And aside from being a good citizen, it's simply too interesting and too much fun to ignore.

We might start by looking at how science gets its facts and at how that process is really one of ignorance generation. From there we can examine how scientists do their work—choosing and making decisions about their careers and the questions they will devote themselves to; how we teach or fail to teach science; and finally how nonspecialists can have access to science through the unlikely portal of ignorance.