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Stalking the Rational Mind

■ Nobel laureate Francis H.C. Crick discovered DNA. Now he's hunting for the very essence of our being--the source of conscious thought.

By Michael A. Hiltzik

His gait is slower now, his voice no longer quite as resonant as the one that used to dominate conversation in sitting rooms around Cambridge, England, in the 1950s, proclaiming his colleagues' errors and oversights and attracting attention like a magnet drawing iron.

"I have never seen Francis Crick in a modest mood" was James D. Watson's appraisal of his research partner in the famous opening line of "The Double Helix," his 1968 memoir of the quest that turned these two young scientists into household names. But time has moderated, if scarcely stilled, the braying laugh that Watson depicted as so penetrating that eminent scientists would flee when they heard it coming down the hall. And Crick's famous habit of haunting other peoples' labs and discerning the importance of their discoveries before they did themselves has diminished, in large part because, at age 86, Crick finds it hard to get around much anymore.

"It pays to sit in on experiments," he says a little wistfully from the dining room of his La Jolla home. "I do go across when I can" to laboratories at the Salk Institute for Biological Studies, where he is president emeritus, and to nearby UC San Diego. "When you go to experimental labs you pick up things about what they're doing that you won't otherwise."

But the traits that made Francis H.C. Crick one of the preeminent theorists of modern science--not to mention one of its premier intellectual provocateurs--are still evident. There is his gleeful pleasure in worrying a scientific problem until it begins to yield, his eagerness to engage experts in a wide range of fields on questions likely to cross the artificial boundaries of individual disciplines, his constant reminders that the role of hypothesis in science is not to isolate an experiment from unexpected paths of inquiry but to provide a rough road map through a murky landscape.

Today, four decades after having won a Nobel Prize and a permanent place in the pantheon of biology for helping to explicate the ancient structure of DNA (the double helix of Watson's book title), Francis Crick is devoting his robust mind to solving a riddle of biology emerging from the opposite end of the evolutionary scale. His goal is to identify the physical basis--the "neural correlate" in scientific terminology--of the very quality that separates humankind from animals and machines: consciousness.

Photos

"Gossip test"
(Marc Lieberman)

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In the last two decades, Crick has become one of the most prolific theorists of this search. In articles, many co-written with Caltech professor Christof Koch, Crick has exhorted his colleagues to explore the physical mechanisms that make us thinking individuals.

At the heart of the Crick-Koch hypothesis is a simple idea with vast implications. It is that consciousness, rather than representing some spiritual or God-given quality, is a biological process like digestion or circulation, generated by the activity of neurons in the brain. As he wrote in his 1994 book, "The Astonishing Hypothesis": "You, your joys and your sorrows--your sense of personal identity and free will, are in fact no more than the behavior of a vast assembly of nerve cells and their associated molecules."

Those words have energized a generation of scientists delving into how neurons communicate with each other and with other structures in the brain and the body. They have produced an explosion of interest in how the electrochemical impulses of millions of organic cells generate images, ideas, desires and memories. "What we've done is make the problem respectable," Crick says, padding around his home, his gangly frame shrouded within a bright knit cardigan. "We nag people."

That's an appropriate way to put it, because within academic circles the scientific study of consciousness was until recently a hard sell. In 1951, when Crick and Watson launched their study of DNA, some molecular biologists thought that the search for the molecular structure was reasonable and the goal attainable. By 1953, DNA's role in carrying genetic information was understood in principle, and several research teams at major universities were racing to decipher its code. Watson later admitted in "The Double Helix" that he assumed that the victors would win the Nobel Prize.

Consciousness is different. Crick acknowledges that consciousness is bound to be a far more complex quarry than DNA. "There are lots of bits of business to explain," he says cheerfully, relishing the sheer intricacy of the quest. "Aesthetic responses to things, long-term plans and so on. The double helix was simple because it goes back to the very beginning of life, when things had to be simple. But consciousness is the product of millions of years of evolution."

Until recently, consciousness remained the exclusive province of philosophers and theologians. They often appealed to concepts such as God or "spirit" to explain the distinction between physical phenomena--say, plant growth or digestion--and mental phenomena such as memory and emotion.

Among scientists, the subject of consciousness carried the scent of the disreputable, similar to studying alchemy or ESP. In academia it was the surest route off the tenure track. Early on, Crick ran up against this prejudice. "An interest in the topic was usually taken as a sign of approaching senility," he recalled in a 1988 memoir. Crick thought it deplorable that science might admit that any physical process was too complicated for scientific research.

Part of his determination derived from the importance of the subject. In the words of Berkeley philosopher John Searle, consciousness is "central ... in the understanding of our very existence as human beings." It plays a role in every phenomenon by which we define our individuality. It includes what it means to see red, feel thirsty, recall the pain of touching a hot grill, suffer grief, find the humor in a pratfall or the joy in love--subjective perceptions that scientists call "qualia." It is what enables a person to assemble a chaos of sights, sounds and smells into the unified perception of an environment, whether kitchen, coal cellar or glade, and distinguish where one's body stops and the rest of that world begins. Or to recognize the face of an aunt or a boss and summon up the appropriate greeting; to decide whether to walk or take a bus; to

judge one's position on a baseball diamond to intercept a batted ball; to plan a shopping trip, a route through the park or a strategy on the battlefield. It is what enables you to read this paragraph, pause, and contemplate what it means to be thinking about thinking.

Consciousness is slower than instinct or reflex but capable of coordinating the actions of a larger number of physical systems. It may be the ultimate example of how nature, starting with the building blocks of biology, can create something of almost infinite complexity.

An early obstacle for scientists was the attempt to define consciousness. By some reckonings there are as many layers of consciousness as there are colors in the spectrum. At the most rudimentary level, consciousness can be regarded as simple awareness of occurrences in the world, perhaps combined with a limited memory that enables animals to respond to novel situations by applying prior knowledge. Researchers have argued that many species can be considered conscious by this definition--ranging from honeybees, which follow their hive mates' "waggle dance" as though aware it leads to food, to dogs who apply their awareness of the difference between strangers and family members to know when to bark out a warning at the approach of intruders.

Humans use the same low-order capabilities to layer meaning onto otherwise random events. "When you touch something hot and pull your hand away, that's a spinal reflex," observes Joseph Bogen, a clinical professor of neurosurgery at USC and visiting professor at Caltech who specializes in split-brain research. "But it's almost always accompanied by a sensation of pain, long after the limb is pulled back." Yet if reflex alone can rescue a limb from danger, why the pain? The answer, Bogen argues, is that consciousness of pain "helps you to learn something that you would not otherwise learn as fast or as well: The next time you're near the stove, you don't touch it."

At the other end of the consciousness scale is what theorists call "higher-order thought"--the self-awareness most people think of as true consciousness. This includes the ability to reflect on one's thoughts and perceptions, to embed them within intricate mental webs of memories and concepts, and to communicate them. Decoding this level of consciousness is "at once the most familiar thing in the world and the most mysterious," writes David Chalmers, a philosophy professor and director of the Center for Consciousness Studies at the University of Arizona. It represents the biggest intellectual challenge for philosophers and scientists alike, with some arguing that it may never yield to human understanding.

One of Crick's most important contributions to the debate has been persuading scientists to set aside temporarily their desire to define the type of consciousness that they are trying to isolate and just start looking. "As a tactical matter it would seem best to discover a lot more" about the neural correlate before trying to refine the search, he says.

"The most valuable thing I ever learned from Francis Crick is not to get mired down in debate but just to focus on what you can agree on," says Bogen, who has devoted much of his 76 years to studying the brain. "If consciousness is everything that everyone wants to apply that word to, the search is hopeless." Bogen interrupts dinner at a Chinese restaurant to hold a teapot aloft. "Almost everybody in this room would agree that this teapot is not conscious. And everyone would agree that everyone in this room is conscious. So there's a reasonable amount of agreement about what we're searching for."

He unfurls a napkin and marks it with a network of interlocking circles, each

representing someone's pet definition of consciousness. Then he indicates the space at the center that falls within every circle. This common element is composed of the subjective perceptions called "qualia"--the sense of red as red, the smell of a jacaranda as a floral perfume or the sun striking our bare arms as a layering on of heat. "That's the crucial, central core of the many various concepts of consciousness," Bogen says.

Researchers already have identified physical manifestations of some phenomena related to consciousness. They have found, for example, that the neural patterns differ when one is viewing an image subconsciously and when one is "seeing" it--actually paying attention. In both cases an image is striking the retina, but only in the latter can a subject describe it. Neurons in parts of the brain also appear to fire in different patterns depending on whether someone is viewing a scene or merely recollecting it (in the mind's eye, so to speak).

These are rudimentary phenomena. Finding the key to higher-level thought is what beckons many scientists in this fledgling discipline. Some argue that as we learn more we will gain a new conception of what it means to be human. Neuroscientists are contemplating the implications of research suggesting that our emotions and personalities are largely manifestations of impersonal electrochemical events in the brain: If we demystify the image of ourselves as entities with free will, if we banish from our culture a conception of the human soul as something spiritual, what kind of people will we become?

Others are starting to consider the ethical and legal questions that could be raised if we learn how to manipulate conscious states. When knowledge of consciousness provides insights into the mechanisms of decision-making, perception and emotion, how much will we be tempted to fix what we consider broken or to "beautify" modes of thinking that are no longer fashionable? Could mental engineering, in the words of the German researcher Thomas Metzinger, "reduce the number of ways acceptable to be a person"? If we conclude that elements of human nature such as moral choice are not the result of a spiritual communion with God and society but the outcome of a hard-wired biology, what will keep us from trying to rewire the system?

There might have been no better candidate to move the subject of consciousness out of the metaphysical world and into the empirical than Francis Crick. Born in 1916 to churchgoing but not especially devout Protestants near Northampton, England, he found himself pondering the incompatibility of science and religion at an early age, and ever after wore his hostility toward religion and philosophy like a badge.

"At exactly which point I lost my early religious faith I am not clear," he wrote, "but it was almost certainly before the actual onset of puberty." To this day, he sprinkles his daily banter with reminders of his antipathy toward philosophers, lest anyone forget that only science holds the key to ultimate truths.

In person, Francis Crick is hardly the figure summarized by Watson in that famous introduction. The tall, slightly stooped figure greeting a visitor to his home exudes charm and an eagerness to engage in dialogue. Silence is scarce in a conversation with him, which is an outpouring of ideas and observations and a challenge to hold up your end of the discussion.

In his memoirs, Crick suggests that Watson misconstrued as immodesty what was really a habit of thinking aloud, an unconstrained emission of ideas expressed "unduly loquaciously." Crick maintains that although his opinions often prove correct in time, they are not always meant as the last word. Rather, they are notions to be pondered, perhaps by more acute minds than his. "For solving protein structures, my point of view was bound to emerge in the long run," he wrote. "By giving my colleagues a very necessary jolt--all I did was help create an atmosphere in which it happened a

little sooner."

Unsurprisingly, these colleagues were often less than grateful. When Crick contradicted the presenters during a postwar Cambridge University colloquium on X-ray crystallography, a topic in which he was a novice, he was charged with the ultimate breach of decorum by a senior scientist: "Crick, you're rocking the boat."

Crick had come to the study of X-ray crystallography by a circuitous route. He says he was never one of those prodigies who settled on his life's work at a tender age. He was an intellectual vagabond, trying on various subjects and gauging his interest by the "gossip test." Whatever topic he gossiped about most was the one that interested him most. From time to time he would be cornered by circumstance into concentrating on one field, and he invariably excelled. Duties during World War II, for example, brought him to a physics lab, where he developed magnetic mines that wreaked havoc on enemy fleets.

War's end found him searching again, his only guidepost a rather broad question. "In the old days I asked myself about very mysterious problems, such as the difference between living things and nonliving," Crick says. Part of the appeal of such arcane study was that it seemed far beyond the scope of modern science. "It was widely believed by educated people at the time that the problems were insoluble."

The question led to two disciplines: neurobiology, the study of the brain, and molecular biology, the study of the simplest components of life.

Neurobiology was at an embryonic stage. Molecular biology, at least, was beginning to solve the riddle of protein synthesis and organization. So he and Watson, his Cambridge research partner, turned their attention to DNA, the chromosomal protein that was known to play a critical role in genetics. Working with the crystallographers Rosalind Franklin and Maurice Wilkins, Crick and Watson discovered the helical structure of DNA in 1953, an achievement for which they and Wilkins won the 1962 Nobel Prize in physiology and medicine. (Franklin had succumbed to cancer in 1958.)

Afterward, Crick dabbled in several fields. As he later wrote, he had started working in molecular biology on the assumption that most of its major questions would outlast his professional life. Instead, by the mid-1960s, most had been solved, including the makeup of the gene and the secrets of its functioning. He toyed with embryology and then with speculations that life on earth had originated from microorganisms sent "by a higher civilization elsewhere," a theory he described as "directed panspermia" in a 1981 book, "Life Itself."

But the gossip test told him his interest was the brain. Having accepted a permanent appointment at the Salk Institute, he decided that determining the physical basis of consciousness would become his new life's work.

What he found was a field that had been all but cowed by philosophical speculation. The 17th century French intellectual René Descartes had staked out the so-called "dualist" position, distinguishing between the body, which was the repository of all things physical, and the mind, which was an ineffable something else. For the next 300 years, anyone who tried to probe the nature of "mind" labored under what might be called the curse of Descartes. You could study the body as a physical manifestation or the mind as the manifestation of an animating spirit, but you could bridge the gulf between them only by appealing to metaphysics.

A wall stood between consciousness and empirical science. If consciousness could not be defined except through first-person reports of subjective phenomena, then it could hardly be an appropriate study for scientists, who were trained to focus only on phenomena that could be observed and verified.

Crick was not dissuaded. He chose to begin by studying vision. The mechanics of vision, how light works on the rods and cones of the eye and is transmitted to the brain via the optic nerve, had been solved. The areas of the cerebral cortex involved in processing visual messages had been located. But obviously there was more to "seeing" than that. "What [was] not yet understood, is how the brain puts all this together to give us our vivid unitary picture of the world," Crick wrote in 1988. This was consciousness, "which one was not supposed to mention."

Crick's first public stab at the subject appeared in a 1979 Scientific American article. He had reached several important conclusions. One was that the study of perception tended to be clouded by subjectivity, which misled researchers into believing that processes such as vision were simpler than they are. What a person senses subjectively when he or she sees, hears, smells or feels is only the output of neurological processes; the processes themselves take place unconsciously. "Our capacity for deceiving ourselves about the operation of our brain is almost limitless, mainly because what we can report is only a minute fraction of what goes on in our head," he wrote.

But that fraction, like everything else, was still the outcome of processes that "involve large numbers of neurons interacting in intricate ways." There was no reason, he concluded, that this neuronal interaction could not be the subject of experimental inquiry.

With Crick's endorsement, the study of subjective states could no longer be dismissed. Crick's argument also concentrated researchers' attention on what could be learned instead of what was beyond the reach of scientific skill. His move to Salk in 1976 had given him a way to do more than exhort scientists in print: He was now in a position to bring like-minded researchers together.

"Francis' style was that when he saw an interesting piece of work, he'd invite the author to visit," says Koch, who met Crick in 1981, thanks to their common interest in studying neural dendrites. Koch says that when he was preparing his first paper on consciousness, he had not received tenure. Crick's agreement to join as a collaborator ensured that the research wouldn't jeopardize Koch's academic career.

Another person drawn into Crick's circle was Patricia Smith Churchland, a Canadian-born philosopher who had approached the consciousness wall from the opposite side. "In 1983, I wrote that we had a lot to learn from neuroscience," recalls Churchland, who later joined the faculty of UC San Diego with her husband, philosopher Paul Churchland. "To philosophers, that was shocking and disgusting. They thought consciousness was either an insolvable problem or strictly an armchair affair, and you would never look at the brain."

Although Churchland believed experimentation on consciousness was still years off, Crick convinced her otherwise. "Francis had thought a lot about the development of molecular biology and science and what you need to frame an attack on a problem. I found myself almost immediately in the mind-set of looking for experiments that would move us along."

Koch, however, became Crick's chief collaborator. The Missouri-born son of German parents, Koch had been educated in Holland, Germany and Morocco as a physicist before landing at Caltech's computation and neural systems program. On the surface, the two men could not be more different: Crick projects a scatter-shot energy; Koch exudes concentration and focus. A dedicated rock climber and devotee of Apple computers (he sports a tattoo of the company's multicolored logo on his right arm), Koch is apt to sustain a conversation while performing casual calisthenics in his Pasadena backyard, a climbing rope coiled over his shoulder.

Every month or so Koch spends a few days at the Crick home, working on his forthcoming book, "The Quest for Consciousness," and engaging in dialogue. As the two men toss ideas back and forth, it seems Koch's role is to keep Crick apprised of interesting fresh research ("Christof does all the hard work," Crick says generously) while Crick provides the intellectual goading that helps drive the field ahead.

"When Francis takes a problem and chews on it and tries this and that, it's a wonderfully creative process," says Churchland. "Christof has some of the same character traits. He's relentless on a problem. Both of them are good at thinking up ideas and quite happy if an idea turns out to be flawed."

If scientists thought that trying to define consciousness waselusive, so, too, have been efforts to identify the physical manifestations they are trying to find. Does conscious thought reside in a discrete area of the brain, resembling the "Broca's area" that is devoted to producing speech? Is consciousness produced by a pattern of electrical impulses, or by a type of neuron that may be found throughout the brain?

Philosopher John Searle says the difficulty arises partly from the undifferentiated structure of the brain: "If you were designing an organic machine to pump blood, you might come up with something like a heart. But if you were designing a machine to produce consciousness, who would think of a hundred billion neurons?"

Indeed, over the years researchers have tried a number of hypotheses. At one point, Crick and Koch speculated that the neural correlate of consciousness might be related to the synchronous firing of groups of neurons at about 40 hertz (40 times a second). To anyone convinced that consciousness involves the high-level coordination of neurons, this was intriguing. But Crick and Koch have more recently backed off some of their broader claims for that theory.

Still, they are inclined to believe that the neural correlate is a discrete process in the brain, whether of neurons acting individually or in groups. "Francis and I believe [it] is probably something very specific," Koch says. "The biological model is very specific--so many things in biology are little machines."

One thing is clear: Crick's interest in consciousness came at a fortuitous moment. Neurologists were just becoming familiar with new tools, including functional magnetic resonance imaging and positron emission tomography, that allow researchers to see which parts of the brain respond to specific stimuli. Implantable electrodes are now sensitive enough to read the electrical activity of individual neurons.

Some neurobiologists believe that some parts of the brain are implicated in consciousness and others are irrelevant. In some cases, fully half of a patient's brain can be surgically removed without rendering the patient unconscious. Conversely, damage to certain tiny structures can place a patient in a lasting coma.

Neuroscientists have identified parts of the brain where specialized processing that may be integral to "awareness" occurs. The cortical region devoted to recognizing faces, for example, is different from the region that responds to images of houses or food. Specialized neural patterns, similarly, appear to come into play when an individual tries to imitate another's action.

Even the most optimistic researchers acknowledge that the science is in its infancy. Among the obstacles is the impossibility of performing invasive experiments on healthy human brains. Instead, researchers look for patients suffering certain kinds of brain damage and compare their responses to various stimuli with those of healthy subjects. Finding the right patients is hard. One researcher recently reported that it

took five years to assemble 20 subjects with damage of a certain kind. A favored alternative is experimenting on macaque monkeys, whose sensory systems resemble humans'--but they can't report on what they feel.

Some think that going after big game like consciousness remains premature. "To do an experiment that goes for the moon wasn't right for our research," says Itzhak Fried, a UCLA neurosurgery professor who has collaborated with Crick and Koch and treats epileptics by implanting electrodes in their brains to stimulate seizure-prone neurons. Fried's precision electrodes allow him to record the activity of individual neurons as his patients view images of faces, food and other items.

When Crick first visited Fried's lab, Fried recalls, "I instinctively thought of consciousness as a quality that seemed too far from our grasp." But he eventually agreed that the opportunity to view the workings of the mind neuron by neuron justified spending time on the big questions. "You can't just look at trivial issues."

Others argue that even identifying the neural correlate of consciousness will not solve the so-called "hard problem"--determining how electrical impulses cause emotions, memories, vision and all of the other phenomena of subjective perception.

Crick is not convinced that the solution is as far off as many colleagues believe. "Once you have what the correlate is, you won't have any difficulty figuring out the cause," he says with a sly smile. "Some philosophers may think it's hopeless. But we think they're just not clever enough."

That doesn't mean he has a glimmer of where the research may lead. It's enough that he has helped start the effort. "Frankly," he says, with the anticipation of a traveler bound for an uncharted realm, "I don't know what the answer is."

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