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Christof Koch's Ascent

Caltech scientist raises consciousness research to respectability | By Karen Heyman

Courtesy of Christof Koch

Scaling what climbers call "big wall," Yosemite's Half Dome appears impossible at the start: A rock face nearly 500 times taller than a person offers only shard-like holds and fingernail-thin cracks for support. But with talent, experience, and enormous focus and discipline, the big wall becomes a series of small, concentrated moves. The climber keeps focused, while the gawkers below admire his courage and question his sanity. California Institute of Technology professor Christof Koch, researcher into the neurobiology of consciousness is an accomplished rock climber.

Koch has ascended the wall of neurobiology for more than a decade. In 1990, he and Nobel laureate Francis Crick challenged biologists' skepticism about studying consciousness. In their 1990 *Seminars in Neuroscience* paper,[1] Crick and Koch swept away centuries of philosophical speculation about the so-called mind/body problem in one stroke of scientific pragmatism: Forget trying to define consciousness, just go out and discover it. As Crick wrote in the preface to *The Astonishing Hypothesis*, the 1994 book that presented their ideas to the lay public: "You do not win battles by debating exactly what is meant by the word battle." But the battle continued: "I would spend the first twenty minutes of ... [a] one-hour talk justifying why I'm not crazy, [that] I'm not with the 'crystal crowd,'" Koch relates.

In his latest book, *The Quest for Consciousness: A Neurobiological Approach*, due out in January 2004, Koch states that he and Crick have revised their earlier proposition that synchronous neuronal oscillations might be at the heart of consciousness. They originally believed that this theory might be the solution to the so-called binding problem: How do differently processed aspects of an object bind together into one percept--red + round + shiny = apple, for example. "Unfortunately, the evidence is slim for a direct relationship," Koch says. "What's much more plausible now is that synchronized firing activity in the 40-Hz range may be necessary to resolve competition.... There's quite a bit of evidence that oscillations might be involved in biasing the selection, but once I'm fully conscious of [the percept], it's unclear whether [the oscillations are really needed.]"

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Koch's previous book, *The Biophysics of Computation*, reflects his background as a physicist, before he turned to neuroscience under mentors Valentin Braitenberg, retired director of Max Planck Institute for Biological Cybernetics, and Tomaso Poggio, now codirector of the Center for Biological and Computational Learning at Massachusetts Institute of Technology (MIT). "Other scientists had ideas about computing in single neurons in the '50s, '60s, and 1970s," Koch says. "I just pushed harder and wrote an entire textbook dedicated to the ideas that ... individual nerve cells are themselves like little computers, quite powerful in their own right."

FOCUS AND DISTRACTION Consciousness inspires a lot of questions about how and why we feel what we do. These questions make for great dorm-room bull sessions, but lousy experiments. Shaking his head over one line of speculation, the effect of self-conscious emotions on behavior, Koch scoffs: "How are you going to study embarrassment in a mouse?"

Crick and Koch have narrowed their approach to the study of awareness, which is the difference between what we do and do not consciously perceive. Given that distinction, distraction itself can become a basis for an experiment. Many of the psychophysics experiments related to consciousness ask that subjects concentrate on only one aspect of a scene; what is then not perceived is remarkable.

Koch acknowledges that his concentration on the visual system might possibly be biased, as he has always been a vision researcher. "There are these beautiful phenomena in vision that allow you to probe the system very deeply, because you can dissociate between what's physically present in the world from what you actually see, and you can do it in a very controlled manner."

In one classic experiment, subjects are asked to count how many times a ball is passed between teams in black and white shirts.[2] The subjects usually don't miscount, but those concentrating on the white shirts often miss a person in a gorilla suit who wanders through the game. Those watching the black shirts are more likely to be alert to a figure dressed in a very different black outfit.

The phenomenon is related to an attribute dubbed "inattentional blindness"[3] after many similarly counterintuitive experiments by other researchers. It is a variant of "change blindness": People notice change if they are already paying attention, but are often blind to superfluous change (the ball-tossing still goes on, gorilla or no gorilla).

Neuronal competition may underlie these results. If rival coalitions of neurons fire at the same time to offer their "interpretations" of a scene, "attentional bias" will determine which interpretation wins. Functional magnetic resonance imaging (fMRI) studies have provided insights into attentional selection. Nancy Kanwisher's lab at MIT has identified visual cortical areas that respond to specific stimuli; for example, the "fusiform face area" responds when subjects view faces.[4] Koch thinks that this kind of specific work in higher cortical areas may lead to discovery of the neuronal correlate of consciousness (NCC), the smallest set of neurons responsible for a particular percept.

Electrophysiology and fMRI experiments by Nikos Logothetis and collaborators[5,6] explore attentional bias by employing binocular rivalry (presenting differing images to each eye). The phenomenon was first observed in the 19th century. A subject will switch back and forth, seeing first one image, then the other. A specific subset of neurons should explicitly code for the "conscious" one.

Experiments also have shown the existence of explicit single neurons in macaques.[7] The monkeys were trained to recognize bent paperclips (chosen specifically because paperclips are not part of a monkey's usual visual experience). An individual neuron would fire in response to a particular clip turned a particular way. In 2000, Koch's then graduate student, Gabriel Kreiman, performed a similar experiment in humans after almost two years of work developing the hardware and algorithms. Kreiman, now a Whiteman Fellow at MIT, and UCLA neurosurgeon Itzhak Fried recorded the activity of single neurons in the brains of conscious patients with epilepsy.[8] The researchers found that one of the neurons was selective to a certain image which happened to be former President Bill Clinton.

Despite these breakthrough experiments, Koch emphasizes that the NCC is not likely to be found at the level of individual neurons. "Single nerve cells are more specific, more particular about stimuli (e.g., the "Clinton" cell) than many psychologists and neuroscientist give them credit," he writes in an E-mail. "It may not require millions of neurons to mediate a specific conscious content (e.g., seeing red or seeing your mom) but maybe only a couple of hundred cells."

Inspired by the work of Robert Clark and Larry Squire that use two forms of Pavlovian conditioning which affect learning,[9] Koch' is collaborating with biologist David Anderson, biophysicist Henry Lester, both at Caltech, and with UCLA behaviorist Michael Fanslow to explore the molecular basis of attention in mice. In Clark and Squire's experiment which used "delay conditioning," the subject hears a tone and then immediately receives an air puff and quickly learns to associate tone and puff. In "trace conditioning" there is a brief interval between tone and puff. Trace conditioning is highly dependent on awareness: Distract a subject, and the association may not be made.

Koch and his collaborators are applying those behavioral techniques to mice, using foot shocks instead of air puffs. Using a combination of genetic and chemical lesion techniques, the group is trying to discover what underlying events occur when a mouse is distracted in the process of learning. Among the highlights of the work: Koch-Anderson postdoc C.J. Han is looking at the effects of chemically induced lesions in the anterior cingulate cortex and immediate early patterns of *c-fos* expression in the mouse brain.[10] Postdoc Eric Slimko is trying to infect mouse neurons with a virus carrying a *Caenorhabditis elegans* gene encoding a channel protein; the effect should be a reversible silencing of the neurons. Postdoc Walter Lerchner is working to identify genes that are differentially expressed in the brain areas of interest, and planning to use one or more of those genes to drive the expression of the silencer gene.

"Correlation is not causation" is the group's mantra. In mice, using molecular techniques, the researchers may finally discover directly

what underlies attention, something not possible with the correlative techniques of fMRI and electrophysiology. Koch sums up the experiment as "a Turing test for consciousness in mice."

Courtesy of Christof Koch

Christof Koch climbing at Castleton Tower in Southeastern Utah with Mensa, a friend's dog.

CRICK AND KOCH, KOCH AND CRICK Their names together may sound like a vaudeville act, but their collaboration has proven an invaluable scientific partnership. When Koch was a young, untenured maverick, Crick's prestige gave credibility and protection to his interest in a then taboo topic. Now semi-retired, Crick writes an E-mail: "Christof is carrying on our joint work. I treat him as an equal, in spite of the difference in our ages. It might perhaps be described as an elder brother/younger brother relationship.... We discuss ideas frequently, either by phone, or during visits [by] Christof to La Jolla. Christof does more of the hard work (e.g., references, checking proofs) than I do. I used to write the first drafts of our joint papers."

They met in 1979, when they both were working on dendritic spines, tiny features of pyramidal neurons through which the majority of excitatory synaptic traffic in the cortex is routed. Then in 1985, Koch wrote a paper on a model of attention[11] that garnered an invitation to visit Crick. Koch says that at the time Crick frequently invited scientists to visit at The Scripps Research Institute "to pump them dry for information. It was very intense."

"What he's looking for is an intellectual sparring partner," Koch adds. "He wants people to be blunt and to be able to take criticism, to put up with him when he says, 'That idea doesn't make sense.'" Yet, unlike other scientists who've achieved iconic status, says Koch, "When you disagree with [Crick] and you have a sensible argument, he's the very first to listen to that."

On a recent visit to Koch's basement office (Caltech has promised for years that he might one day see sunlight), the opera *Orpheus and Eurydice* plays in the background. That Koch, a climber stuck in a subterranean room, might identify with Orpheus--renowned for his talent, idealism, and the courage to take on the king of the underworld--one does not doubt. But Orpheus lost his beloved wife Eurydice for turning to see if she was really behind him as they both escaped Hades. One trusts that Koch, as both climber and scientist, will never look back. Unless consciousness proves to be a function unique to biolipid membranes, he says, "In forty years, we as a civilization will be able to build a machine that's conscious."

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