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Q & A

Christof Koch

Christof Koch is an American neuroscientist best known for his studies and writings exploring the brain basis of consciousness. Trained as a physicist, with a minor in Philosophy, Koch was a Professor of Biology and Engineering at the California Institute of Technology in Pasadena for 27 years, studying the biophysics of cortical neurons and circuits, selective visual attention in the mammalian brain and in machines, the neural mechanisms underlying visual consciousness, and the responses of individual neurons in the medial temporal lobe of patients (i.e., the discovery of the 'Jennifer Aniston' neurons). He is now Chief Scientist and President of the Allen Institute for Brain Science in Seattle, leading a ten-year, high-throughput effort to identify cell types in the mouse and human cortex and to build observatories to map, analyze and understand the structure and function of the neocortex.

Photo © Allen Institute.

What drew you to your specific field of research? An early fascination with analog (yes, I'm that old) and digital computers and how they process sensory information in ways that are similar to and different from the way nervous systems do so. This fire was further kindled by encountering the neuroanatomist Valentin Braitenberg and his wonderful short book *On the Textures of Brains: An Introduction to Neuroanatomy for the Cybernetically Minded*, which drew me into neuroscience. When I became a coder for one of the world's few (at the time) computational neuroscientists, Tomaso Poggio, my fate was sealed.

I was fortunate to obtain my PhD under both Poggio and Braitenberg, analyzing structure–function relationships in the dendritic trees of distinct retinal ganglion cell types, at the Max Planck Institute for Biological Cybernetics in Tübingen (Germany). Thirty-five years later, I have returned to this question, but I've brought along several hundred other scientists, engineers and technicians to help.

Tell us about your switch from academic science at Caltech to 'big science' at the Allen Institute. The traditional scientific endeavor is based on one or a few intellectually gifted and driven individuals discovering new facts about the universe and conceiving of theories to accommodate and explain these facts. For certain projects in more mature disciplines, such as particle physics, cosmology and, yes, biology, this model has reached its limit. This is because of the size and cost of the necessary instrumentation (particle accelerators, telescopes, microscopes) and/or the vast complexity of the system under investigation (embodied by the sheer, uncountable number of degrees of freedoms of even 'simple' model organisms).

After more than a quarter of a century running a laboratory with two dozen graduate students and post-doctoral fellows, and enjoying it intensely, I was ready for a new challenge. I wanted to explore a new model of brain science, including its funding, its organization and its sociology.

Do you have scientific heroes? Yes, I have two real and two imaginary heroes: Albert Einstein, for the way he employed pure thought experiments to build one of the great intellectual edifices of humanity — the theory of general relativity; Francis Crick, for the way he guided molecular biology in its giddy race to discover the universal code of life, for his empirical, pragmatic approach to studying consciousness, and for his uncompromising attitude to life in the face of adversity (he literally dictated corrections to our final paper, on the function of the claustrum, on his deathbed); Sherlock Holmes, for his mastery of abductive reasoning in the service of solving crimes; and Zeno, a physician-cum-alchemist modeled on the historic Paracelsus. Zeno, in Marguerite Yourcenar's *The Abyss*, is living through the earliest phases of market capitalism and the scientific revolution, still rooted in the Scholastic, but struggling to emerge into the more rational view of the universe of the Enlightenment.

Which historical scientist would you like to meet and what would you ask her/him? I would like to ask René Descartes "Comment modifieriez-vous vos idées concernant *res cogitans* et *res extensa* à la lumière de la neuroscience moderne?"

If you would not have made it as a scientist, what would have been an alternative career? To search for extraterrestrial intelligence using artificial intelligence.

What's your favorite experiment? Alan Hodgkin and Andrew Huxley's elucidation, using the voltage-clamp recording technique, of the biophysical mechanisms underlying the initiation and propagation of the action potential in the squid giant axon, using primitive recording equipment and pharmacology. They formulated a phenomenological model that quantitatively reproduced their observations in terms of the interaction between a sodium, a potassium and a leakage current. They solved these equations on a hand-cranked calculator, taking three weeks (sic) to compute the numerical value of the propagation speed of the action potential, which was within 10% of the observed value! I am in awe of this achievement, which required exceptional analytical and intuitive skills. Suitable versions of these Hodgkin–Huxley equations continue to be in use today, 66 years after their data and models were published.

What are some of the biggest challenges facing biology? Two out of three experiments in the biomedical sciences — cancer biology, neuroscience, psychology, etc. — cannot be reproduced. This replication crisis can't be elided and goes to the heart of science. Yet most scientists continue to ignore these uncomfortable facts.

How can this be addressed? Four positive measures to address some of the root causes of this crisis are: focusing on a handful of agreed-upon model species and breeds; using validated standard operation procedures; carrying out large, comprehensive surveys; and making all data and associated metadata, Jupyter Notebooks, and so on, openly available. This is what we are practicing at the Allen Institute.

It is imperative that all data and computational procedures be freely, openly and universally shared. This remains a promissory note for most published studies, which is strange, as the vast majority of biomedical science is funded by the public purse or by charities.

What is your greatest research ambition? To build and operate a 'brain observatory' that routinely, reliably and reproducibly records widespread neural activity in the brain of the laboratory mouse using cellular-level optical and electrophysiological techniques, under a variety of canonical sensory-motor behaviors. All data and metadata will be analyzed using published standard operating procedures and made openly available. Just like in astronomy, interested scientists will apply for time on this observatory, and, in a competitive process, the most interesting experiments will be chosen.

What do you think is the biggest problem neuroscience as a whole is facing today (besides the above mentioned replication crisis)? As the study of brains has matured from its romantic, provisional phase into an established science, with ca. 60,000 professionals and a voracious appetite for funding, the public expect some return on this investment in terms of therapies for many of the neurological and psychiatric conditions the brain is prey to.

What is your greatest passion? To understand how the brain — the most complex piece of highly organized matter in the known universe — gives rise to conscious experience. Why not the liver or the heart — two other important organs? What is it about the physics of the brain, subject to the same laws as everything else, that transforms electrical activity in a subset of neurons into feelings?

If you could ask an omniscient higher being one scientific question, what would it be and why? Courtesy of Isaac Asimov, I would ask, "Can the workings of the second law of thermodynamics be reversed?" For, if they can, we and the universe can live forever.

If I could sneak in a second question, it would be, "Why is there something rather than nothing?"

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Quick guide

Insect jumping springs

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How do some insects jump so quickly? As anyone who has tried to catch a grasshopper or a planthopper knows, many insects can jump very rapidly. A planthopper can accelerate in less than 1 millisecond to a take-off velocity of 5 m s^{-1}, requiring a power output (energy per given time) of tens of thousands of Watts per kilogram of muscle. To do this, jumping insects have to overcome two mechanical limitations. First, the maximum mechanical power a muscle can produce is only approximately 300 W kg^{-1} and furthermore, the faster a muscle contracts, the less force it can generate, exacerbating the problem. Second, a jumping animal can only accelerate while it remains in contact with the ground: in most small insects, therefore, the length of the propulsive legs determines the time available to reach a given take-off velocity. Some larger insects, like katydids, use the leverage provided by their disproportionately long legs to multiply the power produced by direct muscle contraction to propel jumps. If the legs are short, however, alternative mechanisms must be used to generate the necessary mechanical power. How do these insects do it? They jump by using springs; devices that allow energy to be stored gradually in mechanical deformations and then released abruptly.

How do springs enable quick jumps? In insects that use springs to jump, the legs are first moved into the same cocked position and the joints locked. The power-producing muscles then contract slowly over periods of 100 milliseconds to a few seconds without moving the legs; instead, the force generated distorts parts of the skeleton, which store mechanical energy. The sudden release of these loaded skeletal springs then powers the rapid propulsive movements of the legs. The elastic recoil of the spring returns the stored energy very quickly. The power is amplified because almost all the energy produced