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A REMEMBRANCE OF ROGER W. SPERRY

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In the era of modern science, it is seldom that anyone ventures far from their field of expertise, and nearly unheard of for someone to make major contributions in such diverse disciplines as psychology and developmental biology. Roger Sperry, who passed away in April of this year, was one of these rare individuals. Sperry received a Nobel prize in 1981 for his "split brain" studies on cortical hemispheric specialization, but there were many who felt he also deserved one for his earlier work on the formation of nerve connections.

The 60's and 70's were a transition time in which both areas were being actively pursued in his laboratory at Caltech and, for those of us in the lab, it was a remarkable experience in scientific cultural diversity. In the "human wing," split brain patients were being tested with everything from exotic image stabilization devices to tinker toys. The rest of the lab contained a veritable zoo. There was a colony of monkeys and cats, mostly with split brains, being tested with elaborate electromechanical devices. There was a room full of newly-hatched chicks pecking bad-tasting beads to study memory formation; and various frogs and fish were having nerves cut to study selective nerve growth using electrophysiological and neuroanatomical methods.

Sperry was happy to let us work on whatever we wanted as long as we could convince him that we were asking an important question. Although he was happy to give general advice about what to do, it was largely up to us to figure out how to do the experiments, and we did so with a great deal of independence. Writing up the experiments, however, was a different reality. Sperry, who majored in English literature as an undergraduate, was an excellent writer and expected every paper that came from his lab to be well written, down to the choice of the best synonym for every word. For those of us who were less gifted writers, this was a traumatic ordeal of endless revisions which could easily last a year or more. The papers and our writing skills, but not our egos, were the better for it. Generously, Sperry did not put his name on most of our papers.

Sperry's contribution to developmental neurobiology was fundamental, but to really appreciate this one has to go back to the late 1930's and early 1940's when he did his work. At that time, it was generally believed that individual nerve fibers were essentially identical in the way they responded to their local environment during axonal growth. Tissue culture studies seemed to show that axons were guided solely by mechanical structures, and a number of *in vivo* studies had purportedly shown that fibers would form connections with whatever targets they were made to encounter. Astoundingly, these misconnected fibers even appeared to support normal function. The conclusion was that nerve fibers were intrinsically identical and that neuronal function depended on learning, not on specific neuronal connections.

Sperry tested this then current wisdom by rotating the eye of a frog by 180 degrees and then cutting and scrambling the optic nerve. When the nerve grew back, he tested the frog's vision by presenting it with a fly on the end of a wire. When the fly was in front of the frog, the frog turned 180 degrees, and when the fly was behind it, the frog snapped as if the fly were in front. The frog saw a visual world upside down, never learning to see correctly. It would have starved if left on its own. From this simple experiment, Sperry concluded that optic fibers from different parts of the retina must

have grown to specific locations in the brain and therefore fibers must possess chemical identities that allow them to differentially respond to different chemospecific cues in the brain. The experiment also showed that specific connections, not just learning, were fundamental for neuronal function.

As a young assistant professor when this pioneering work was done, Sperry showed remarkable courage, considering that his thesis advisor and colleague at the University of Chicago, Paul Weiss, was the major proponent of mechanical guidance. Perhaps too much courage, because in spite of having published a number of papers extending and confirming his early findings in several different systems, he was denied tenure. (Chicago later gave him an honorary degree.) At Caltech, Sperry continued this work, culminating in the early 60's with direct anatomical evidence for the directed growth of optic fibers and the elaboration of his chemoaffinity hypothesis.

Today, the idea that growing axons differentially respond to chemical cues in their environment to form specific connections during development and that specific connections are actually important for neuronal function is hardly controversial. It is a fact of life for developmental neurobiologists. Many examples of selective growth have been reported in diverse systems from mammalian cortex to *Drosophila* nervous system, and a few guidance molecules have now been identified. It is good to remember that there was a time that we did not know about chemospecificity and that it was Roger Sperry who told us about it.

Note: Ron Meyer was one of Roger Sperry's last graduate students

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