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Biophysicist in Profile

Henry Lester

Henry Lester, the Biophysical Society's newly-inducted President, has always been fascinated by gadgets and how they work. So when, at a high school science fair, he heard research scientists say that the brain was the most complex gadget of all, his imagination was captured. He needed to know, at the most basic level, how the brain works.

That lifelong enthrallment with gadgets leads Lester to correlate the progress of his career with the size of computer he used for research. As a Harvard undergrad studying chemistry and physics (a neurobiology major did not yet exist), he worked at a particle accelerator, programming in FORTRAN on a computer that filled an entire building. Graduate studies in biophysics found him in the lab of *H. K. Hartline*, *Floyd Ratliff* and *Frederick A. Dodge* at the Rockefeller University. Hartline, who had just won the Nobel Prize for his pioneering discovery that eyes use a code consisting of nerve impulse frequencies, employed the first online computer for electrophysiology—a computer which, Lester says, “merely filled a room.”

After doing his postdoc work at the Institut Pasteur in Paris, Lester started his own lab at the California Institute of Technology, where he remains as the Bren Professor of Biology. When his lab opened in 1973, he notes, “electrophysiology was still the only quantitative way to approach neuroscience, but progress allowed me to install a ‘minicomputer’ in a single cabinet.” In 1981, he and colleague *Jerry Pine* received Pasadena's first IBM Personal Computers, which, he says, “we happily integrated into our electrophysiology rigs.” As PCs continue to shrink, Lester jests that he looks forward to someday running experiments with his cell phone.

Best known, perhaps, for his landmark work on various ion channels and receptors—including identification of a specific nicotine receptor protein, called an alpha4 subunit, as key to addiction – Lester's career is marked by originality and productivity. In addition to an array of research interests, Lester also writes journal reviews, serves on four editorial boards, reviews grant proposals for the NIH, holds eight US patents, has published more than 240 scientific papers, recently served as Chair of Caltech's Faculty Senate, and taught required freshman biology to Caltech non-biologists.

Despite the breadth of his interests, Lester does not appear to lose his focus or leave a work unfinished. His first NIH grant is now in its 33rd year, and the California Tobacco-Related Disease Research Program has funded Lester's research for all but two of the past 18 years. Lester and his colleagues look forward to better drugs becoming available for smoking cessation, as well as safe ways to exploit the “broad therapeutic hint” from the inverse correlation

between tobacco use and Parkinson's disease. "If present hypotheses pan out," Lester says, "we may soon understand the molecular, sub-cellular, cellular, and circuit-level changes that occur in response to chronic exposure to nicotine." One such hypothesis: chronic nicotine becomes a "pharmacological chaperone" for its own receptors, "a topic important to study with biophysical rigor."

Dennis Dougherty, Hoag Professor of Chemistry at Caltech, knows Lester as "an enthusiastic and generous collaborator," noting that Lester's wide range of interests and talents enable him to interact with many different kinds of scientists. "He brings first-rate scientific standards, creativity, and an ability to see how different viewpoints can make the whole greater than the sum of the parts." That perspective engendered his receiving a 2008 McKnight Technological Innovations in Neuroscience Award. The grant supports unique approaches to understanding the brain and the development of technologies that will be made available to other neuroscientists.

Princess Imoukhuede, a graduate student in Lester's lab from 2003 to 2008, was inspired by his ability to make the theoretical real and to ask the right questions to get to the heart of any experiment. She watched with fascination the first time she saw Lester and a postdoc take apart a physiology rig, examining PMTs, lenses, and any component of interest—asking as he worked if she understood why he checked components. "I found it exciting to participate in science that required me to understand fundamentally each system, each instrument, and each process I was studying or using," says Imoukhuede, who carries the approach with her as a postdoctoral fellow at the Johns Hopkins University School of Medicine.

Alan Finkel, now Chancellor of Australia's largest university (Monash), began working with Lester 25 years ago. As founder and CEO of Axon Instruments Inc., Finkel tapped Lester's vast scientific technology skills to help grow Axon into the world's leading supplier of electrophysiology equipment and software. Finkel

remarks that on consultant visits, "Henry consistently allowed extra time to spend with the engineers discussing their projects and, most importantly, giving them context to help make their design projects more relevant and hence more exciting." Finkel recruited Lester to join his company's Board of Directors as their only external director, because "Henry's advice was always sage and fearless."

Busy as he is, Henry Lester also enjoys physical and social activities, often with his family. When his son, Ben, was "a taciturn teenager," Lester found SCUBA diving to be the perfect bonding activity. "Underwater, you don't have to try to talk to each other; you just flash each other the occasional OK sign." Now he tries to work out frequently with his wife, Margaret, who is a nurse practitioner in pulmonary disease.

When Lester isn't traveling for science conferences or visiting one of his children—Ben, a science journalist, or Beth, a market research director—he often bikes to and from work.

Assuming leadership of the Biophysical Society at "the worst funding environment in 40 years," he urges pressing for President Obama's pledge to "restore science to its rightful place" to include expanded support for basic biomedical research. "*Roger Tsien's* Nobel Prize and *Steve Chu's* appointment as Energy Secretary," he continues, "bathe all us biophysicists in a bit of reflected glory. Importantly, their success also creates opportunities; we need to use our enhanced stature to work on research, education, advocacy and outreach." He also wants to ensure that foreign members of the Society see themselves as valued and important. "Gadgets are fun," he says, "but empowering people to produce better science is the best goal of all."



Henry Lester boating.