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# On the training of future neuroscientists: insights from the Grass Laboratory

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## Abstract

The understanding of nature is a continuous process that requires the transference of current knowledge to future generations. In this article, we address the critical issue of training of future scientists, an essential aspect of scientific progress. As an example of the impact training programs can have on shaping future scientists, we focus on the experience of the Grass Laboratory, which provides early career investigators the opportunity to embark on independent research experiences. This uniquely designed program has contributed enormously to fostering the development of neuroscientists in the past 60 years and has left a recognizable mark on 20<sup>th</sup> and 21<sup>st</sup> century neuroscience research.

## INTRODUCTION

"Nothing is so dangerous to the progress of the human mind than to assume that our views of science are ultimate, that there are no mysteries in nature, that our triumphs are complete and that there are no new worlds to conquer."

Humphry Davy, 1810.

Scientific research is an endless journey of discovery that necessarily requires the transference of current notions and research tools to future generations of scientists. Scientific articles are commonly focused on descriptions of new experimental data or highlight the contributions of individual investigators. On the other hand, one of the most critical components of scientific progress, the training of future scientists, is rarely discussed. Training in the scientific method traditionally occurs at several levels, including courses at the undergraduate and graduate levels and less formal postdoctoral training. Hands-on specialty courses do exist (e.g., Woods Hole, Cold Spring Harbor), but few academic institutions offer similar formal courses, and training in experimental techniques is

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usually left to the laboratory of the sponsoring investigator. In this article, we consider the importance of training the next generations of scientists, focusing on the Grass Laboratory as a prominent example of a complimentary approach to scientific education that has had a profound impact on a number of early career neuroscientists. The program provides a forum for neuroscientists to carry out their first independent research work in an environment consisting of peers at similar stages of their scientific careers. Thus, the Grass Laboratory is unique in its class, complementing and enhancing formal training by stimulating the imagination and creativity of neuroscientists early in their careers.

Capturing the essence of Einstein's insightful thought: "*It is a miracle that curiosity survives formal education and yet it is the supreme art of the teacher to awaken joy in creative expression and knowledge*" (Einstein and Calaprice, 1996), the Grass Laboratory hosts between 8 and 12 fellows during 14 weeks in the summer in the highly stimulating environment of the Marine Biological Laboratory in Woods Hole, Massachusetts (Figure 1) This unique designed program targets promising new investigators that are at the "critical period", when the possibility of becoming their own principal investigator during the summer will contribute to developing the necessary self-confidence and drive to pursue an independent research career. This "critical period" usually takes place during the late postdoctoral years but the program is also appropriate for advanced graduate students and new Assistant Professors. Fellows are responsible for administering their own summer research (e.g. animal protocols, research budget, equipment selection and installation) and are generously supported by the Grass Foundation and by a range of companies that provide much of the equipment and software necessary to conduct cutting-edge research.

Why is this program at the Marine Biological Laboratory? In our opinion, there is not a better place to expose beginning neuroscientists to the excitement of research than the Marine Biological Laboratory (MBL). Founded in 1888, the MBL is a private, not-for-profit corporation and is home to scientists who are recognized authorities in their fields. The 270 year-round scientists and staff are joined each year by more than 400 visiting scientists, summer staff, and research associates from hundreds of institutions around the world. Among the scientists with a significant affiliation with the MBL are 54 Nobel Prize winners, 196 Members of the National Academy of Sciences, and 171 Members of the American Academy of Arts and Sciences. Resonating with Humphry Davy's conception of science, the MBL embraces the philosophy that "the single greatest discovery is the realization that every discovery paves the way to future discoveries" (http://www.mbl.edu/videos/). The MBL is not only recognized for the quality and contributions of its researchers but also for its commitment to the education of students. Its outstanding educational programs include a variety of world-renowned summer courses focused on various biological disciplines, and hundreds of scientists from around the world come to Woods Hole during the summer to engage in the research and educational activities of the MBL.

The study of the nervous system at the MBL was first recognizable in 1891 by Herbert Henry Donaldson's presentation of a talk entitled: "Methods of Studying the Nervous System" (Maienschein, 1990). Subsequently, Charles Otis Whitman (a zoologist who made major contributions in the areas of evolution, embryology and animal behavior), the first MBL director, asked the comparative anatomist Howard Ayers to organize a neurological

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seminar. During the nineteenth century, comparative anatomical analyses in fishes and amphibians led to major breakthroughs in the understanding of the vertebrate nervous system. Although the seminar continued for only three years, 1896–1898 (Maienschein, 1990), the interest in neurological work has continued at the Marine Biology Laboratory. Notably, the studies on the Limulus lateral eye by H. Keffer Hartline in the 1920s and 1930s provided a plethora of insights into the basic mechanisms of visual function. His work on the neurophysiological mechanisms of vision in horseshoe crabs earned him the Nobel Prize in 1967, which he shared with George Wald and Ragnar Granit. Stephen Kuffler, who later founded the Department of Neurobiology at Harvard University, arrived at the MBL for the first time during the summer of 1947 and began studies on the stretch receptor of the lobster and crayfish (Kuffler, 1954; Barlow, 1993). However, it was J. Z. Young's "rediscovery" of the squid giant axon that led to an enormous growth in neurobiology at the MBL (Young, 1936; Young, 1938). The MBL provided a home for the investigations of Kenneth S. (Kacy) Cole in squids that resulted in the voltage-clamp technique and elegantly documented the change in membrane conductance that occurs during the propagation of action potentials along the axon (Cole and Curtis; 1939). The 1950s, 60s and 70s saw an ever-increasing diversity in approaches to the study of the nervous system that attracted a new cadre of scientists and the development of new summer courses at the MBL. The numbers of MBL scientists studying the nervous system grew from 24 neurobiologists in 1954 to 110 in 1970 (Kravitz, 2004). During those years, Rodolfo Llinás (Llinás, 1999) and George Augustine (Augustine et al., 1985a,b; Smith et al; 1985) greatly contributed to our understanding of Ca<sup>++</sup>-dependent mechanisms of neurotransmitter release with their studies in the squid giant synapse, and Clay Armstrong set the basis of our current understanding of ion channel structure and function (Armstrong, 1969)..

#### History of the Grass Fellowship

Albert Grass, a part time engineer in the Department of Physiology at Harvard University, was contracted by Frederic Gibbs to build the first multichannel EEG machine in the USA (Zottoli, 2001). Ellen Robinson, a neuroscientist, and Albert Grass met at Harvard Medical School, married and as the demand for EEG machines and other electrophysiological equipment grew, they founded the Grass Instrument Company, and their success provided them with the means by which they could give back to the scientific community. Alexander Forbes, a Harvard neuroscientist, provided the first connection of Albert and Ellen Grass and The Grass Foundation to the exciting growth of neurophysiology at MBL (Zottoli, 2001). Starting in 1951, Albert and Ellen Grass developed a fellowship program for investigators to conduct independent research for the summer at the MBL (Zottoli, 2001). This generous, and visionary, decision gave birth to a unique training program.

Harry Grundfest (Columbia University), Stephen Kuffler (Harvard University), and Ichiji Tasaki (National Institutes of Health) played a crucial mentoring role in the early years of the Grass Fellows program, and therefore could be considered the first "directors" of the program. Early in the 1970's, the program was formalized with a Director, Donald T. Frazier (Grass Fellow in 1967), and a dedicated space ("Grass Laboratory"), designed for maximum interaction between laboratory members (Figure 1), was established.

The administration of Grass Laboratory Program has evolved over the years to include a Director, who oversees the daily operation of the laboratory and facilitates contacts between fellows, and resident and visiting researchers, and an Associate Director, who helps Fellows find the appropriate resources. Many companies generously provide cutting-edge loaner equipment that allows fellows to propose and conduct research that would be difficult to accomplish at their home institutions. With the growth of the interdisciplinary approaches to the nervous system, The Grass Foundation began supporting projects in neurophysiology, biophysics, integrative neurobiology, neuroethology, neuroanatomy, neuropharmacology, systems neuroscience, cellular and developmental neurobiology, and computational approaches to neural systems. Despite the evolution of the Grass Fellowship Program, one constant over the years has been the availability of the broader MBL community to help mentor and guide the fellows. It is during the Grass Fellowship that many fellows form their peer-networking group and where many fellows meet the leading scientists in their respective fields. The number of Grass Fellows now exceeds 600 and many have made significant contributions to the neuroscience (Fig. 2) in the twentieth and twenty-first centuries (a full listing can be found at: www.grassfoundation.org). All former Grass Fellows have developed over the years a lifelong connection to the MBL and a valuable network of colleagues and potential collaborators.

#### The training of future scientists and its present challenges

Natural science is the quintessential expression of the human experience, and has invaded and transformed human life through the medium of industry (Marx, 1844). In the first decade of the twenty-first century, most industrialized nations realized the importance of science for maintaining their relative economical prevalence. These nations focused their investment in scientific research by initiating programs centered on commercially motivated technological innovation and by orienting biomedical research funding agencies towards disease-centered initiatives. Thus, the funding for basic science has been dramatically reduced, challenging the very basic concepts of science itself. Far from the wonder of nature and the pursuit of knowledge that characterized science since the times of Humphry Davy (Holmes, 2008), contemporary science seems too focused on the potential commercial value of the data obtained. As a result of these policies, the funding for biomedical research has become more limited towards goal-oriented research rather than towards exploration (Morrison, 2010). This has the effect of stifling innovation and transformative discovery, yet represents a current research reality.

Such focus on goal-oriented research represents, in addition, a serious challenge for the training of future neuroscientists. In these times of exceedingly large science administration and where scientific success is measured in a dollar value, there is little room for simple scientific curiosity and creative experimentation. As a consequence, the current funding policies do not only impact trained scientists, which pragmatically adapt to this new reality without compromising basic scientific principles, but potentially the formation of new scientists which will be trained under questionable scientific pretenses. Despite its limitations science is the most precious thing mankind has (Einstein and Calaprice, 1996) and the only tool available to explore the natural laws that govern the universe, whose complexity we only superficially understand. Reducing science to a simple problem-solving

exercise might be convenient in the short-term, but is potentially dangerous for the progress of society at large. Furthermore, while profitable in economical terms, some industry and government initiatives and approaches might not be necessarily scientific in nature.

Perhaps the most important challenge of our time is thus how to secure the transfer of knowledge and true scientific values to future generations in a society where science has increasing economical value. This is why the emphasis and commitment of organizations such as the MBL and the Grass laboratory with scientific training take a new dimension and particular importance, providing enclaves for the dissemination of science. The Grass Fellowship Program has responded to this shift in the research community and initiated changes that extend the value of the program beyond benefits resulting from the scientific growth of the fellow to also support the home laboratory. Many fellows now continue their home project, ensuring ongoing progress of research programs at home. The fellows also have access to state-of-the-art instrumentation and experimental model systems that might not be available at home institutions, helping to obtain critical data for papers and grant applications. Additionally, scientific interactions with other researchers at the MBL lead to possible collaborations and enhancement of research programs. Thus, from both the fellow's and the home laboratory's point of view, the fellowship is a win-win opportunity.

In contrast to previous scientific revolutions whose audience was reduced to a small elite group of scholars, the romantic British scientific revolution of the late eighteenth and early nineteenth centuries (in which Humphry Davy participated) inaugurated the commitment to communicating results and to educate society at large (Holmes, 2008). Honoring this belief, the Grass Fellowship Program has and will continue to evolve to match the rapidly changing neuroscience discipline and the needs of scientists early in their careers while maintaining, in spite of circumstantial funding trends, the core scientific values and uncompromised passion for discovery which characterized romantic science.

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## Figure 1. Marine Biological Laboratory (MBL) in Woods Hole

<u>Top</u>: View of the MBL and Eel pond. <u>Bottom left</u>: The Lillie Building where the first Grass Laboratory was located. <u>Bottom right</u>: the Rowe Building, home of the current Laboratory.

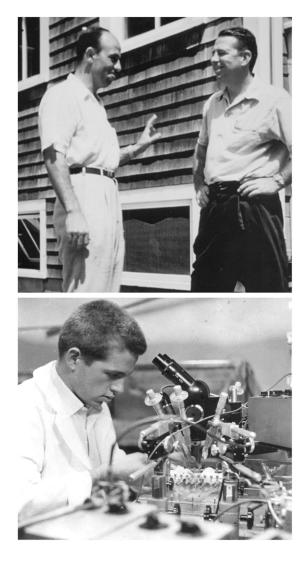


Figure 2. The Grass Laboratory played a decisive role in the scientific career of many leading neuroscientists in the field of synaptic transmission

<u>Top</u>: Fellow Ricardo Miledi with Albert Grass at the MBL in 1955. The Grass fellowship was transformative for Miledi, seeding his interest in the role of Ca<sup>++</sup> in synaptic transmission. In collaboration with Bernard Katz and Paul Fatt (Katz, 1969), Miledi later provided major contributions to our understanding of mechanisms of transmitter release and pioneered the use of frog oocytes to study native receptors and express exogenous messenger RNA. <u>Bottom</u>: Fellow Michael V.L. Bennett in 1958, recording from supramedullary cells in a puffer fish. Bennett's investigations while a Grass Fellow led to one of the first demonstrations of electrical coupling between vertebrate neurons. He later contributed to the detailed characterization of this modality of synaptic transmission, which is mediated by membrane specializations known as gap junctions. Michael Bennett's seminal observations defined this field of research, in which he is the unequivocal world's expert.