State-of-the art (Arnold) behavioral neuroendocrinology

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The Daniel S. Lehrman Lifetime Achievement Award in Behavioral Neuroendocrinology for 2010 was presented to Arthur P. Arnold at the Society for Behavioral Neuroendocrinology (SBN) meeting in Toronto, Ontario, Canada in July, 2010. Art obtained his A.B. in Psychology from Grinnell College in 1967 and his Ph.D. in Neurobiology and Behavior from The Rockefeller University in 1974. He remained at Rockefeller for postdoctoral studies before joining the Department of Psychology at UCLA as an Assistant Professor in 1976. Art advanced rapidly to Full Professor by 1983 and, since 2000, he has been Distinguished Professor of Physiological Science, a department now called Integrative Biology and Physiology. Art’s numerous and diverse contributions to the field of behavioral neuroendocrinology make him a superb choice for this prestigious award. He played a key role in shaping the field of behavioral neuroendocrinology and making SBN one of the most successful organizations in the fields of behavioral neuroscience and neuroendocrinology.

Art as a Scientist

Art is a prolific researcher. He has generated an impressive publication record of over 225 papers with the majority published in top-tier journals. There may be no better way of illustrating Art’s impact on the field of behavioral neuroendocrinology than simply listing some of his most significant contributions.

• 1976—with his Ph.D. mentor Fernando Nottebohm, first demonstrated sex differences in the brain at the light microscopic level in a vertebrate, in the bird song control system (Nottebohm and Arnold, 1976). That same year they demonstrated accumulation of steroid hormones in that song system (Arnold et al., 1976).
• 1979—demonstrated large sex differences in hormone accumulation in vertebrate neurons (Arnold and Saltiel, 1979).
• 1980—with his first graduate student Marc Breedlove, established the spinal nucleus of the bulbocavernosus (SNB) as a major model system for studying mammalian sexual differentiation and steroid effects on neurons during development and in adulthood (Breedlove and Arnold, 1980).
• 1984—with his postdoctoral fellow Sarah Bottjer, established the importance of the magnocellular nucleus of the neopallium in learning, but not maintenance of bird song (Bottjer et al., 1984).
• 1985—with his postdoctoral fellows Ernie Nordeen, Kathy Nordeen and Dale Sengelaub, provided the first proof that sex steroids prevent normally-occurring neuronal death in a vertebrate and established this mechanism as part of the process of sexual differentiation of the central nervous system, thereby explaining, at least in part, the nature of the critical period for brain sexual differentiation (Nordeen et al., 1985).
• 1986—with his postdoctoral fellows Elizabeth Kurz and Dale Sengelaub, first demonstrated in adult mammals that sex steroids regulate dendritic growth and reorganization in steroid-sensitive neurons (Kurz et al., 1986).
• 1989—with his graduate student Cynthia Jordan, first demonstrated that sex steroid hormones regulate developmental synapse elimination (Jordan et al., 1989a,b).
• 1992—with his postdoctoral fellow Barney Schlinger, first demonstrated that the brain can be the major source of plasma estrogen in a male vertebrate (Schlinger and Arnold, 1992).
• 1996—with his postdoctoral fellow Juli Wade, demonstrated that large amounts of testicular tissue fail to masculinize neural development in the zebra finch brain, arguing against a mechanism of sexual differentiation based solely on testicular secretions (Wade and Arnold, 1996).
• 2002—assembled an international team of researchers that developed the “four-core genotype” mouse model to study relative contributions of sex hormones versus direct effects of sex chromosomes on sexual differentiation of the brain (De Vries et al., 2002). Using this model, Art and his postdoctoral fellow Laura Carruth and their collaborator Ingrid Reisert demonstrated a sex
chromosome effect on neuronal sexual differentiation in vitro (Carruth et al., 2002).

- 2003—with graduate student Bob Agate, former postdoctoral fellow Bill Grisham, and collaborators, obtained convincing evidence that genetic sex contributed to sexual differentiation of the songbird by analyzing the brain of a rare lateral gynandromorphic (half male, half female) zebra finch (Agate et al., 2003).

- 2006–present—with colleagues in the “four-core genotype” mouse project, first demonstrated sex chromosome effects on not only aggression, pain, addiction-related habit formation, and neural tube closure defects, but also autoimmune disease and hypertension (Gatewood et al., 2006; Quinn et al., 2007). This demonstrated the use of this model to study sexual differentiation in general.

- 2007—with postdoctoral fellow Yuichiro Itoh, graduate student Esther Melamed, and colleagues, performed the first global analysis of avian sex chromosome dosage compensation, showing poor compensation relative to that of mammals (Itoh et al., 2007).

- 2009—with graduate student Atila van Nas, colleague Jake Lusis and others, first analyzed sex differences in gene networks identified by untutored bioinformatic methods (Van Nas et al., 2009).

This list illustrates that Art has constantly brought fresh ideas and introduced modern techniques into the study of brain sex differentiation, thereby having propelled it into a popular field of investigation worldwide. Research laboratories all around the globe study sex differences in bird song control systems and the SBN, and if they study other sex differences, they are likely to consider approaches or interpretations pioneered by Art. He challenged the dogma that gonadal hormones create all phenotypic sex differences by demonstrating the contributions of genes encoded on the sex chromosomes to the differentiation of sexually dimorphic neural as well as non-neural traits. By extending his research beyond neural realms Art is helping to change our views of sexual differentiation of the entire body.

One example of Art’s tenacity and flexibility came from his realization that, in zebra finches, gonadal steroid hormones were likely not entirely responsible for creating their obvious sex differences in adult singing behavior and in the adult neural song circuitry (circuits that he helped describe and deciper). At that time, a few mammalian studies had produced data suggesting that some brain sex differences arise autonomously from inherent genotypic sex-differences. To investigate this possibility in birds, Art required expertise in molecular genetics, so in his 40s and 50s, he became a “graduate student” all over again. He spent sabbatical periods in the lab of Tony Campagnoni at UCLA, and of Andrew Sinclair in Melbourne, Australia where, back at the lab bench, he worked long hours to develop molecular resources for studying sex differences in zebra finch brain. He re-educated himself through extensive reading and discussion, especially with Paul Burgoyne in London. By these efforts, Art transformed into a world leader in the biology of vertebrate sex chromosomes and in the genetics of sexual differentiation.

Art has a superb intellect giving him the capacity to absorb and process data from disparate fields and synthesize this information into big-picture ideas. In addition, Art is a scientist of unparalleled precision. He spends a great deal of time and effort mastering all the techniques used in his lab. When new equipment is purchased, he is often the first reading through the manual, learning all the details for its operation, calibration and maintenance. Before any experimental data is collected involving new procedures in his lab, Art painstakingly works with his lab members to optimize experimental conditions and to define procedural limits. Once data are collected and before any publications emerge, Art is cautious in interpreting the results and conservative in the generalization of these results to theory.

Art as Mentor, Leader and Friend

Those who have worked with Art also know him to be an exceptional mentor, teacher and role model. Over the course of his career he has graduated 12 Ph.D. students and 23 postdoctoral fellows. Due in large part to his guidance, many of his scientific progeny have gone on to faculty positions and have themselves become leaders in behavioral neuroendocrinology. Although he maintains an extraordinarily busy schedule, he still finds time to engage with all of the members of his lab, including his undergraduate students. Art’s weekly lab meetings are so engaging and scientifically worthwhile that they are attended not only by members of his own lab but also by undergraduates, graduate students and post-docs from a variety of different laboratories at UCLA.

Throughout his career, Art has generously assumed numerous positions of leadership in his service to the scientific establishment. When the Society of Behavioral Neuroendocrinology was founded, Art was a logical choice for its first President. He was also the inaugural Secretary for the Organization for the Study of Sex Differences (OSSD), and is currently Editor-in-Chief of a new journal, Biology of Sex Differences, the official journal of the OSSD. Since 2005, he has been the Director of the Laboratory of Neuroendocrinology at UCLA, a University-wide consortium of scientists with interests in behavioral and genetic neuroendocrinology.

Art will never be known as chatty. However, get him on the subject of sexual differentiation (or perhaps provide a snifter of Lagavulin) and he can talk your ear off. With his serious demeanor and his significant stature (Distinguished Professor at 6’3”), Art can be intimidating to younger scientists. To ease the tension Art skillfully injects humor into his interactions with students and colleagues alike. His exceptional wit makes him deceptively funny. This humor and his mischievousness that makes you realize (in case you’d forgotten or didn’t know) just how much warmth and humanity lies at his core. These qualities are especially evident in his devotion to his family. Indeed, the only thing more important to Art than sexual differentiation is his family. He has been married to Caroline Arnold (an award-winning author of children’s books) for 43 years. His two children Jennifer and Matthew are highly successful professionals (one a professor of psycholinguistics, the other a practicing neurologist). Both are also parents, making Art the grandfather of $n = 3$.

Through the years we have all had the honor of becoming acquainted with many outstanding scientists. Some became our mentors, some our collaborators, and some our friends. We are most fortunate that Art chose to pursue a career in behavioral neuroendocrinology so that he could assume all three roles in the lives of all of us devoted to this engaging field of study. For all these reasons and more, Art is richly deserving of the Daniel S. Lehrman Lifetime Achievement Award in Behavioral Neuroendocrinology.

References


