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Sir Vincent Wigglesworth and the coming of age of insect development

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ABSTRACT Sir Vincent Wigglesworth (1899-1994), a founder of the discipline of Insect Physiology, was a central figure in the emergence of the concept of postembryonic insect development as sequential polymorphism regulated by endocrine signals. At a time in mid-century when genetics and developmental physiology were severely compartmentalized, he made the conceptual linkage with the recognition that sequential polymorphism must have a genetic basis with gene activation regulated by internal signals.

KEY WORDS: *sequental polymorphism, rhodnius, brain hormone,moulting, hormone, juvenile hormone*

The 'whys' and the 'hows' of insect metamorphosis have challenged great thinkers since the dawn of recorded scholarship. Aristotle, William Harvey, Swammerdam, Darwin and August Weismann all had their interpretations. A thread that runs a tortuous course from Aristotle's time through the 19th century, visualizing the insect larva and pupa as active embryos was broken by Darwin, who saw the relationship of larva and pupa to the adult insect as a polymorphism with successive adaptive functions, the larva to sedentary feeding and the adult to reproduction, with the pupa as a bridge passage. That concept of metamorphosis as sequential polymorphism finally crystallized out to a spare sentence: *Metamorphosis is merely one type of polymorphism* in Wigglesworth's slim monograph "The Physiology of Insect Metamorphosis" (1954). Polymorphism in its many guises is everywhere, as Darwin noted, but it is in the great diversification and evolutionary success of the insects that sequential polymorphism finds its fullest expression as a life history strategy first to eat and grow, and then to disperse and reproduce. That solved the 'why' problem.

The 'how' problem too had explanations to fit the models of the times ever since antiquity. Ovid in "The Metamorphoses" presents the teaching of Pythagoras thus: "...if you select bulls, kill them, and bury them in a trench, from every part of the rotting carcasses will come bees....a war-horse covered with earth produces hornets...the farmers know full well that the worms which spin a cocoon of white threads on the leaves in country places, change into butterflies... mud contains germs that produce green frogs..." (Ovid, 8). Weismann (1864), who first fully recognized the function and significance of the imaginal discs, illustrated 100 years earlier by Lyonet (1762), saw them from the perspective of the then newly promulgated Cell Theory. But the mechanisms of molting and postembryonic development remained mysterious even long after the importance of hormones had been recognized in the vertebrates. Perhaps because of the absence of significant effects of larval gonad removal on the secondary sexual characters of adult insects, it was concluded that insects, in contrast to vertebrates, lacked hormones. Kopec's (1922) experiments, leading to the then heretical proposal that the insect brain secreted a hormone responsible for metamorphosis, opened the book to the final chapter in the endocrine physiology of postembryonic development of insects, and yet it was to take another thirty years before a coherent theory emerged. The subject had attracted many skilled experimentalists in the years following that first postulate that nerve cells could secrete and that hormones might regulate postembryonic development, but it was V.B. Wigglesworth who brought together his own brilliant experiments with the work of others, from the 1930's to the 50's, to present the first synthesis that finally gave a mechanistic answer to the 'how' question of postembryonic development in insects.

Wigglesworth, who was born in 1899, began his research career at the London School of Hygiene and Tropical Medicine in 1926 with a medical degree and a life-long love of insects. By 1939 he had completed the first edition of what was to become the bible of a new discipline: "The Principles of Insect Physiology" (Wigglesworth, 1939), and to go through 8 editions. Its preface begins: "Insects provide an ideal medium in which to study all the problems of physiology" (development, as he saw it, is a branch of physiology). He went on to demonstrate the truth of that postulate, attending to several different systems, and making important discoveries in all of them, but it was on the question of postembryonic development that he made the most important advances. He died in 1994, three years after the publication of his 264th paper, and after a lifetime that spanned the rediscovery of Mendel's papers, the triumph of the Neuron Doctrine, the founding of the disciplines of Biochemistry and Genetics, the birth of neuroendocrinology and of molecular biology, the solution of the genetic code,

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Sir Vincent Wigglesworth in his laboratory, probably in the 1980s. (Courtesy of Peter Lawrence).

and the metamorphosis of developmental physiology into developmental genetics. It has been said of Alexander von Humboldt that he was the last person to know all of science. So it is that Wigglesworth was probably the last person to know all of insect physiology.

In these days of rapid progress with powerful but largely mechanized techniques it is salutary to reflect on the hard-won results of earlier generations where individual technique and thoughtful, creative experimental design were the keys to progress. Wigglesworth's science epitomized the best of this approach, for which I shall give some examples. But before doing so I shall digress briefly to explain how I chose to enter the field of insect physiology since I think it may be not atypical. My own epiphany came as an undergraduate with the discovery of Wigglesworth's (1953) paper on the origin of sensory neurons in *Rhodnius*, published in the Quarterly Journal of Microscopical Science (now metamorphosed into Development). This paper showed the cell lineage and pattern of differentiation of the four components of a sensillum - the bristle cell (trichogen), the socket cell (tormogen), a neuron and a glial cell, from an epidermal cell, not for the first time - Kohler (1932) did that - but with clarity and accessibility. Recent intensive genetic analyses (reviewed in Jan and Jan 1993) are the heirs of such studies. In a small colonial Zoology Department where dusty vertebrate comparative anatomy reigned, my introduction to the seeming simplicity and tractability of the insect, as revealed by Wigglesworth's paper, with its clear, direct prose and elegant, spare line drawings was the conversion experience. Robert Frost, the American poet, has said that a poem should begin in delight and end in wisdom. On that basis it might be claimed that many of Wigglesworth's best papers were poems of development.

Rhodnius prolixus, a blood-sucking ectoparasite of mammals and birds, and vector of the trypanosome that causes Chagas' disease in central America was in culture when Wigglesworth arrived to take up his first position in the department of P.A. Buxtont. It soon became almost synonymous with Wigglesworth as it became his experimental insect, first in studies of excretion, but from 1933 on, in studies of molting and postembryonic development. He recognized that *Rhodnius* is superbly designed to be an experimental insect: as an immature insect it takes a large blood meal and then molts a precise number of days later, it has cuticular markers that distinguish immature from adult cuticle, and in the right hands it can be joined in parabiosis to others, even of very different stages and with animals that have been deprived of the brain and/or the nearby endocrine glands, the corpora allata. These qualities of the experimental insect in combination with Wigglesworth's innovative skill in microscopy yielded a rich stream of papers throughout seven decades, with few digressions to other insects. With *Rhodnius* he first showed by implantation experiments that protocerebral neurosecretory cells were the source of the hormone that initiates the molting cycle (Wigglesworth, 1939). This finding, building on Kopec's, was the first experimental demonstration of an endocrine role for neural cells in any animal. The cue for the release of this hormone in *Rhodnius* was proven to be the large blood meal, for cutting the ventral nerve cord in the thorax after a blood meal prevented the expected molt. (Wigglesworth, 1934). But there was evidence too that the brain hormone did not act directly or alone on the epidermis; he showed that a decapitated fourth instar larva, induced to start the molt cycle by parabiosis to a similar larva that had passed the critical period for initiation of the molt, could then be joined in parabiosis to a further decapitated larva and thereby induce molting. This was taken to imply that the molting tissues could in themselves provide a humoral stimulus but it subsequently turned out that a second endocrine center, the thoracic glands (Fukuda 1940) was involved. By the 1950's this two-stage system had been confirmed in many different insects. From the first simple, ingenious and telling experiments to the isolation of the brain hormone peptide (now the prothoracicotropic hormone) and of ecdysone from the prothoracic gland is a story told many times, but which can be savored from Wigglesworth's several reviews (Wigglesworth 1954, 1959,1964) and from more recent reviews, e.g. Nijhout (1994).

But molting and growing are not the only processes to need explanation: what regulates maturation and metamorphosis in insects? The first indication that the assumption of adult features (metamorphosis) was under control from the head again came from decapitation experiments with *Rhodnius* (Wigglesworth 1934). Insects that were deprived of endocrine glands attached to the brain (the corpora allata) underwent a precocious molt to the adult state, while implantation of corpora allata from juvenile stages ensured a juvenile molt. Thus the third one of the major developmental hormones - the juvenile hormone - was recognized and the triumvirate has since been demonstrated in innumerable insects. The composition and modes of action of the three insect hormones has, of course, become a major effort of insect developmental biology (Nijhout 1994).

As I have noted elsewhere (Edwards 1994), Wigglesworth did not achieve the resolution of the 'how' questions alone. The reference list in his 1954 monograph lists such eminent figures as Bodenstein, Bounhiol, Fukuda, Hadorn, Karlson, Kopec, Kuhn, Pflugfelder, Piepho, and Williams. His contribution, beyond his own experiments, and the creation of insect physiology as a discipline, was to integrate a coherent view of the process of postembryonic development as a sequential polymorphism played out through the multiple capacities of the epidermis as it passes through a series of molts that are orchestrated by the endocrine system.

Wigglesworth also introduced us to the extraordinary capacities of the epidermal cell in its secretory cycles, wound healing and pattern formation. He postulated a model for the spatial distribution of new sensilla as the insect grows through successive molts,

Portrait of Sir Vincent Wigglesworth by C.B.Freeth. This painting can be seen in the library of the Zoology Department in Cambridge. (Courtesy of Peter Lawrence).

based on the concept of inhibitory gradients around existing sensilla (Wigglesworth 1954,1961a). These models of the social functions of epidermal cells, largely brought to light by simple but clever experiments have become part of the conceptual foundation on which today's molecular approach is founded (e.g., Blaumueller and Artavanis-Tsakonis 1997) As with good buildings, unless one looks for the foundations one does not see them.

This volume celebrates a pioneer of developmental genetics, the father of the compartment concept (García-Bellido *et al.,* 1973). The advance of developmental genetics in the last 20-30 years has been so rapid that it is surprising to look back to the 1960's and see how compartmentalized the subject of development then was. Genetics was largely the study of mutants, developmentalists generally looked at other things, among them the endocrine control of development. It is instructive to return to a symposium on insect polymorphism (Kennedy 1961), where two eminent geneticists, E.B. Ford and T. Dobzhansky, address the theory of genetic polymorphism and the dynamics of chromosomal polymorphism in *Drosophila* respectively without a nod to the developmental implications. It was for Wigglesworth in his concluding synthesis (Wigglesworth 1961b) to step out of the developmentalists compartment and attempt an interpretation of sequential polymorphism in genetic terms: "...*it seems reasonable to suppose that the entire structure of the normal adult is determined by the action of one set of genes (many of them without known alleles) and the structure of the normal larva by another set of genes. That is the same phenomenon as that postulated to account for the different parts of the body. Both differentiation and metamorphosis can be regarded as polymorphisms with a genetic basis evoked by appropriate stimuli from the internal*"

While that simple model, based on two sets of genes, one for the larva and one for the adult, has proven to be too simple since it is now clear that the same genes act under different controls in larva and adult alike, it was a significant step because it helped to bring about an awareness that developmentalists and geneticists had to look at the question through each others' eyes.

I have quoted his conclusion to the same paper (Wigglesworth, 1961b) elsewhere, but it seems most appropriate in this volume to conclude with his statement of faith: "*No one is a more ardent enthusiast than the convert; he may be an embarrassment to his new friends; he is liable to be more loyal than the king. Perhaps I am in that state with respect to genetics. Forsaking the old and widely held belief that genes are concerned only with certain limited characters which geneticists are pleased to study, I have now come to the point where I feel that every feature of the animal has a genetic origin.*" Contemporary developmental genetics surely justifies his intuition.

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