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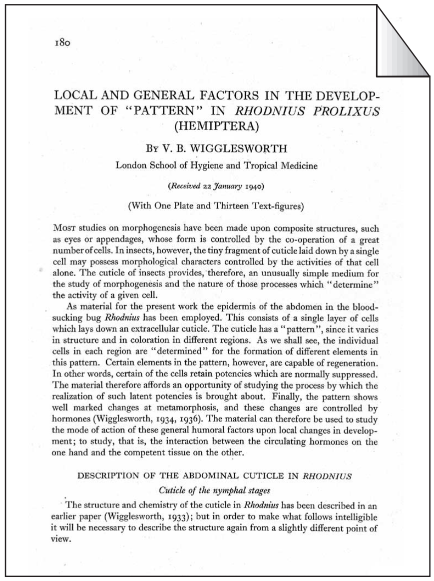
JEB Classics

A WIGGLESWORTH CLASSIC: HOW CELLS MAKE PATTERNS



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LOCAL AND GENERAL FACTORS IN THE DEVELOPMENT OF "PATTERN" IN *RHODNIUS PROLIXUS* (HEMIPTERA)

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(*Received 22 January* 1940)

(With One Plate and Thirteen Text-figures)

Most studies on morphogenesis have been made upon composite structures, such as eyes or appendages, whose form is controlled by the co-operation of a great number of cells. In insects, however, the tiny fragment of cuticle laid down by a single cell may possess morphological characters controlled by the activities of that cell alone. The cuticle of insects provides, therefore, an unusually simple medium for the study of morphogenesis and the nature of those processes which "determine" the activity of a given cell.

As material for the present work the epidermis of the abdomen in the blood-sucking bug *Rhodnius* has been employed. This consists of a single layer of cells which lays down an extracellular cuticle. The cuticle has a "pattern", since it varies in structure and in coloration in different regions. As we shall see, the individual cells in each region are "determined" for the formation of different elements in this pattern. Certain elements in the pattern, however, are capable of regeneration. In other words, certain of the cells retain potencies which are normally suppressed. The material therefore affords an opportunity of studying the process by which the realization of such latent potencies is brought about. Finally, the pattern shows well marked changes at metamorphosis, and these changes are controlled by hormones (Wigglesworth, 1934, 1936). The material can therefore be used to study the mode of action of these general humoral factors upon local changes in development; to study, that is, the interaction between the circulating hormones on the one hand and the competent tissue on the other.

DESCRIPTION OF THE ABDOMINAL CUTICLE IN *RHODNIUS*

Cuticle of the nymphal stages

The structure and chemistry of the cuticle in *Rhodnius* has been described in an earlier paper (Wigglesworth, 1933); but in order to make what follows intelligible it will be necessary to describe the structure again from a slightly different point of view.

Peter Lawrence writes about V. B. Wigglesworth's 1940 publication 'Local and general factors in the development of 'pattern' in Rhodnius prolixus *(Hemiptera)'. A pdf file of Wigglesworth's paper can be accessed as supplemental data at jeb.biologists.org*

In January 1940, London was not the most peaceful place in the world, but it was in that month that V. B. Wigglesworth, known to entomologists as VBW, submitted one of his best papers to *The Journal of Experimental Biology*. VBW was an exceptional scientist in many ways. He was original, reflective and a superb experimentalist, and made the field of insect physiology almost single handed. He published 264 papers (all but a few, single author works) and wrote 9 books (including the renowned work, *The Principles of Insect Physiology*) in a long life (Lawrence and Locke, 1997; Locke, 1994). He was not a salesman — yet he wrote his papers in a simple and direct style that a first year student could understand. It is hard to think of anyone who was more unlike most successful modern scientists, yet who made so many important discoveries. This paper, 'Local and general factors in the development of 'pattern' in *Rhodnius prolixus* (Hemiptera)' (Wigglesworth, 1940), epitomises what was unique about his scientific approach.

He was working on *Rhodnius*, a blood-sucking bug (Hemiptera, Reduviidae) and decided to think about 'pattern formation', a subject that was pursued by perhaps 10–20 people in the world at that time. Pattern formation had really been recognised as a specific problem by German embryologists and was a straight translation of their word Musterbildung. How were the tissues of an animal marshalled and directed so that they could construct the body? VBW realised the advantages offered by the insect epidermis. At a time when most were concerned with abstract embryological concepts such as fields and competence, morphollaxis and epimorphosis, VBW saw clearly an elemental truth. In his 1940 publication, he argues that patterns derive from the diverse behaviour of ***single*** cells — "*the tiny fragment of cuticle laid down by a single cell may possess morphological characters controlled by the activity of that cell alone*". He harnessed this hypothesis to his knowledge that the insect epidermis is a monolayer and was set to make his observations and use his head.

Scientists find their questions from different sources and many, too many I think, look in the literature, they listen into the gossip of the day and deal therefore with fashionable concerns. There is another way, and this is the route followed by VBW. He let the material ask the questions. Looking carefully at *Rhodnius* he noted many features: the sensory bristles, the pattern of pigment and the muscle insertions. He thought about the cuticular pigmentation; for example, was something indelible written into the cells that secreted it — would they carry the potential to make pigment if they were forced to divide? In the manner of J.-H. Fabre, he intervened in a simple and direct way to answer the question. Early in the 1940 paper, he describes how he burnt the cells located nearby to a pigment spot, forcing the pigmented cells to divide as they migrated in to heal the wound. When the next cuticle was laid down, he found the pigment spot to be enlarged and deformed, arguing that the pigmented cells were determined and had handed on their state to their daughter cells.

Why are the adult and juvenile patterns so different? VBW had already discovered juvenile hormone, and he knew that this hormone acted as a switch; if it was present juvenile structures were made, if absent then the adult pattern. Were all cells capable of responding to the hormone, or did they have to be primed? VBW took grafts of epidermis from younger larvae and transplanted them onto metamorphosing nymphs; he also moved them from place to place. He concluded that cells in different places were already differently determined in respect of both larval and adult pattern.

He also noted that one moult after a burn, the bristles were missing, but in the next moult they were regenerated. He commented: "*It is worth noting that, with few exceptions, the regenerated… bristles show the normal orientation. This raises a new problem which has not been further investigated*". He later thought about planar polarity a little more (Wigglesworth, 1959) but did not return to it again. Perhaps wisely, because it is still a mystery; even now we still don't know what a bristle cell reads to tell it where anterior is. VBW made a door-opening observation, there is an interesting room behind it, but, still, 63 years on, there is too little light to see inside.

Next, he turned his attention to something else: he noticed that the bristles were evenly spaced. Because the bristles reappeared *de novo* after a burn he deduced that epidermal cells were transforming themselves into bristles, a conclusion that fitted well with the work going on at that time in Germany about the development of scales in moths (I think the earliest paper on the scale cell lineage is Stossberg, 1937). The accuracy of the spacing suggested that the epidermal cells are sensitive to their position relative to extant bristles. Looking at normal development he found that, as the insect grows, new bristles are added, and again they are not added at random but tend to appear in the largest spaces between the pre-existing ones. By a series of simple experiments and logical deductions he concluded that the important variable was not the distance between pre-existing bristles, but the number of cells. How was the number of cells to be measured? Here VBW proposed a "*working hypothesis*" in which a gradient molecule would be made by all the epidermal cells; it would be absorbed by pre-existing bristles but be necessary for engendering new ones; its concentration would only be sufficient to sponsor new bristles at sites far away from the others. He was fully aware that his simple idea could be the basis of a more general and molecular model of positional information (a term to be coined in 1969; Wolpert, 1969) and he compared it to models of pattern formation in hydroids and worms. Indeed Morgan had proposed the idea of a morphogen much earlier (Morgan, 1897), although his model was different to how we look at morphogens now (Lawrence, 2001). VBW's observations were also the beginning of studies that led to understanding of lateral inhibition, the function of Notch and much besides.

I don't think VBW would have relished reading the current literature, even those many papers that contain both ideas and data that followed from his observations. Although he read enormously and was encyclopaedic in his knowledge he did not enjoy papers that had to be decoded before they could be understood, nor did he think it proper for scientists to advertise themselves, or steal credit from others. Locke compared him to a type of butterfly that has only been seen once: "*Wigglesworth was just such a unique specimen. His achievements came from a man, a time and an opportunity that can never be repeated*" (Locke, 1994). But his approach can be instructive; read this 1940 paper and learn that the material you study can be a better guide at suggesting original questions than a visit to the library.

10.1242/jeb.00775

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