HPLS (2017) 39:30
DOI 10.1007/s40656-017-0157-y

ORIGINAL PAPER

Homage to Eric Davidson

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Published online: 16 October 2017
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Abstract The Britten–Davidson model of genetic regulation was well received by American molecular biologists and embryologists, but not by the members of the French School of molecular biology. In particular, François Jacob considered it too abstract and too removed from experiments. I re-examine the contrast between the Britten–Davidson model and the operon model by Jacob and Monod, the different scientific contexts in which they were produced and the different roles they played. I also describe my recent encounters with Eric Davidson, and how I discovered the extraordinary continuity of his work on the development of the sea urchin, as well as his rich personality.

Keywords Embryology · Evolution · Gene regulation · Microbiology · Systems biology

I met Eric Davidson quite late in my career. The first encounter was in Beer-Sheva during one of the meetings organized by Ute Deichmann at the Jacques Loeb Centre for the History and Philosophy of the Life Sciences. Before then, I had known of Eric through his work—first his articles written in the 1960s and then his book published in 1968 on molecular embryology. They revealed the dramatic changes in gene expression and RNA populations during the early stages of embryogenesis. They also confirmed, for higher organisms and their development, the main results obtained in bacteria. Most importantly, they showed that there were new phenomena occurring during the development of higher organisms that had not been anticipated, such as the observation that some messenger RNAs were pre-stored in the oocyte and their translation was activated during the early developmental stages. Recently,

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I wrote an article stating that these early publications of Eric were a third pillar of molecular biology, after the discovery of the structure of DNA and of the genetic code, and the characterization of the regulatory mechanisms controlling gene expression in microorganisms (Morange 2009).

Eric's results were very important in attracting molecular biologists, who until then had been working on bacteria and bacteriophages, to the study of higher organisms and of their development.

My second scientific encounter with Eric's work was the famous model of gene regulation in higher organisms that he proposed in 1969 with Roy Britten in the journal *Science*. I was trained in the French school of molecular biology and I have to acknowledge that this paper was not well received by French researchers. It will probably surprise many, but up to the end of his life François Jacob had the feeling that the value of the operon model had not been fully acknowledged. Not the value of the model in explaining genetic regulation in bacteria, but the efforts that Monod and he had made at the conclusion of the Cold Spring Harbor meeting in 1961 to adapt the operon model to account for gene regulation in higher organisms, particularly during their development. Jacob had the feeling that this part of their work had been ignored. When the first developmental genes were isolated and characterized at the beginning of the 1980s, in particular the homeobox-containing genes, and were shown to encode transcription factors, this demonstrated for Jacob that the hypotheses that he and Monod had proposed in 1961 were correct. But there was no reference to these early models in the numerous articles published in the mid-1980s. In addition, Jacob did not like the Britten–Davidson model. He found it too speculative and believed that it did not pay sufficient tribute to the operon model. I shared these opinions: it is always difficult for a young research trainee not to adopt his school's opinions!

This is why I was so happy, when I co-organized a meeting at the Pasteur Institute in Paris to commemorate the Nobel Prize awarded to Lwoff, Monod and Jacob, to ask Eric to come and to speak about his own model of gene regulation and to compare it with the operon model and its extensions. He agreed and I thought that it was the right time to compare the strengths and weaknesses of the two models and to estimate their relative roles in the rise of a molecular explanation of development. Unfortunately, Eric passed away before this meeting, so we will never have his retrospective point of view on the relative value of these two models.

Personally, I think that the two models were complementary, pointing to different aspects of gene regulation during development. The Monod–Jacob model was important because it underlined that the main level of gene regulation during development is, as in bacteria, the control of gene transcription, and that proteins directly control this process by binding to DNA. The Britten–Davidson model was also important because it emphasized that the phenomenon of gene regulation during development had to be considered in a more global, holistic way, as it is now in the gene regulatory networks progressively drawn up by Eric in recent years. Two years after they proposed their model, Britten and Davidson also did something that Jacob and Monod did not: they established a connection between the structure of these gene regulatory networks and evolution. Regulatory circuits evolved and their transformation was the motor of organismic evolution.

The later work done by Eric Davidson—the description of the logic of complex promoters and enhancers binding so many different transcription factors, the description of gene regulatory networks, their modelling, and the demonstration of the value of these models—is well known. I will not say any more because there are specialists here that know far more than me about this part of Eric's work. I would just like to say that it also had a huge impact on historians and philosophers of science, after Evelyn Fox Keller devoted a chapter of her 2002 book to Eric's work (Keller 2002).

As I mentioned previously, I met Eric some years ago, and in conclusion I would like to outline four characteristics of his personality that struck me.

The first was his enthusiasm, despite his impaired mobility. This enthusiasm never faded as he neared the end of his life: quite the contrary, in fact. It was fascinating to see the progression of his work year after year, the increasingly global view he had of the regulation of gene expression during development.

The second characteristic was already mentioned by Ellen: his ambition, not only to uncover new scientific facts, but also to present a new view of scientific phenomena, to position his results in a broader perspective. In this, I would compare his attitude to that of Ernst Mayr. I don't know whether Eric would have appreciated this comparison because his relations with evolutionary biologists were not always harmonious. But he did for molecular and developmental biology what Ernst Mayr did for evolutionary biology: he showed that the scientific developments in which he participated were inscribed in the history of biology and led to a "growth of biological thought" in the words of Ernst Mayr.

The last two characteristics of Eric that I want to mention were shared by François Jacob. Such a parallel might appear strange after what I said previously, but I am convinced that despite distinct scientific conceptions, their personalities were not so different.

The first was Eric's capacity to refuse a new model or a new hypothesis if he believed that it was not valid, and even to be aggressive if a scientist was unable to explain the objectives of his own experiments properly. Eric, like Jacob, expressed very strong opinions about people and their experiments!

I will mention one last characteristic that both researchers shared and that might appear contradictory, but was in fact complementary. Unfortunately, many scientists of great stature become superficial with time; as their honors and accomplishments mount they become unable to establish deep intellectual relationships with others. They play a role, as if they were actors in front of cameras. This was not so for Jacob, nor for Eric. When Eric appreciated somebody he had the ability to nurture a strong intellectual relationship with the person. When Eric discussed something with you, you had the feeling that the conversation was important to him, that he wanted to know what you thought, and to convince you. He looked at you intensely, showing that he was fully engaged in the conversation.

The discussions of this type that I had with Eric at the meetings organized by Ute were all too rare, but I know that I will always remember them.

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