Obituary

Walter Gehring (1939–2014)

Eric Wieschaus¹ and Christiane Nüsslein-Volhard²

Walter Gehring died on May 29 at the age of 75 following injuries received in a car accident several weeks earlier while on vacation in Lesbos, Greece. Gehring was one of the most influential and significant developmental biologists of the past 40 years. He did his graduate work at the University of Zürich with Ernst Hadorn and began his independent career as an assistant professor at the Yale Medical School in New Haven, Connecticut, in 1969. He returned to Switzerland in 1972 to head the Cell Biology Department at the Biozentrum in Basel, where he remained until his death.

Walter Gehring played a pivotal role in the renaissance of developmental biology in the last quarter of the 20th century. His lab, which over three decades housed an inordinate number of later renowned biologists, pioneered the application of molecular biology techniques to Drosophila development. These efforts culminated in the identification of the homeobox — a remarkably conserved DNA binding element that is found in transcription factors across all animals. Homeobox-containing proteins often act as developmental ‘master regulators’ in a very similar fashion in evolutionarily distant animals, a fact betrayed by the spectacular finding from Gehring’s lab that the vertebrate eye regulator PAX-6 can initiate eye development in fruit flies. Such a deep evolutionary conservation of molecular mechanisms of development had not been expected, and Gehring’s contribution to its discovery was major.

Walter Gehring started his graduate works with Ernst Hadorn (1902–1976), the eminent Swiss developmental geneticist who was intensely interested in the mechanisms that control cell fate during development. Drosophila was an ideal organism for these studies, not only because of its well established genetics, but because groups of cells called ‘imaginal discs’ could be identified in the larva that appeared undifferentiated but were already programmed to form specific parts of the adult fly. Hadorn’s lab had shown that specific imaginal discs would maintain their programming even when cultured in vivo for long periods of time in the abdomen of adult Drosophila females. There were striking exceptions, however: when allowed to differentiate after transplantation into larvae that underwent metamorphosis, future leg cells, for instance, could occasionally ‘transdetermine’ to form wing and other structures. In his thesis work, Gehring showed that transdetermination could also occur in antennal imaginal discs, such that future antennal cells would form leg like structures after culturing and metamorphosis. By using mitotic recombination to label the progeny of individual cells, he showed that the transdetermination process, although it resembled a spontaneous mutation, was not strictly clonal and often occurred in groups of neighboring cells. These experiments were a technological tour-de-force and suggested that cell fate decisions might involve cell interactions.

During his graduate work in Zürich, Gehring chanced upon a mutation in Drosophila that produced antenna to leg transformations similar to those he had observed in culture but this time in intact animals. He called his mutation ‘Nasobemia’ after an imaginary creature walking on its nose described in a poem by Christian Morgenstern and maintained a special affection for that locus throughout his subsequent scientific career. He believed that the antenna-to-leg transformation reflected a master regulatory role for the affected gene, and that the failure to maintain particular activity states of the gene might explain transdetermination. How proliferation and neighbor cell interactions affect the determined states of cells remains an interesting and unsolved problem in developmental biology. Walter returned to the problem in a famous paper (Chan and Gehring (1971) Proc. Natl. Acad. Sci. USA. 68, 2217–2221) from his period at Yale in which he showed that cells cultured from anterior fragments of the Drosophila blastoderm retained their anterior programming and formed antennal structures even when mixed in close juxtaposition with cells from other regions of the embryo. These experiments provided the first evidence that cells in the fly embryo were already

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From above: Satellite images help researchers to monitor the health of crucial ecosystems, such as coastal mangrove wetlands. This false composite Landsat 5 image shows Mnazi Bay, between Tanzania and Mozambique. (Image: Clare Duncan, Zoological Society of London.)

and time. However, it’s not all about machines taking over from field workers. Technology can also help to get more people involved with field work in ecology and conservation.

The Earthwatch Institute (www.earthwatch.org), for instance, supports a project called My Tree Tracker, based on a smartphone app encouraging volunteers to keep an eye on the growth and health of the trees in their cities. Just by recording very simple datapoints including the location, species, and circumference of trees in their neighbourhood, people can make a valuable contribution to ecological studies characterising the ‘urban forest’, which in turn helps to make modern cities a healthier and friendlier environment. In 2012 and 2013 Earthwatch engaged over 300 volunteers to measure over 5,000 trees in four US cities, including Cambridge (Massachusetts), San Francisco, Chicago, and Atlanta, and the organisation is aiming to expand the project further.

Overall, from simple free apps and recycled smartphones through to drones and satellites, modern technology offers many tools that can help ecologists and conservationists with their work. As Nathalie Pettorelli concludes: “Satellite remote sensing, camera traps, microphone arrays, guided drones, Doppler radar: these are all becoming central to our ability to understand and manage our natural world”.

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programmed to specific fates at the undifferentiated blastoderm stage. Like all of Walter’s early work, they pointed to the existence of genetic mechanisms directing cells to specific fates, but what was frustrating at the time was the difficulty of getting at the underlying mechanism.

During his two years as postdoc with Alan Garen, a famous biochemist at Yale who, as many molecular geneticists at the time, had become interested in development, Walter tried his hand at biochemistry, isolating DNA binding proteins from imaginal discs in a hope to identify cell fate regulators that distinguished cells destined to form wings, antennae and legs in the fly. These experiments were not successful and ultimately were abandoned for the more cell biological approaches that represent his best work from Yale. In some sense, they were too simple and too optimistic given the technologies available in the late 1960s and early 1970s. But Walter clearly appreciated the value of getting a molecular handle on developmental decisions. His stellar early career resulted in a full professorship at the age of 33 at the newly founded Biozentrum, an interdisciplinary modern university institute in Basel, Switzerland, his home country, where he stayed from then on.

By the time Walter moved to Basel, a general strategy for cloning genes had been established, and the era of recombinant DNA had arrived. The move to the Biozentrum gave him an opportunity to restructure his lab towards molecular biology, with the aim of identifying the molecular mechanism of determination. Neither of us, however, directly contributed to this approach in his lab. Eric Wieschaus, who was Gehring’s first graduate student and followed him from Yale to Basel, had focused his thesis on cell lineage analyses, while Christiane Nüsslein-Volhard, although a trained molecular biologist, had started in the Gehring lab as a postdoc to screen for maternal mutants affecting embryo development.

Cloning and analyzing developmental genes became the research focus of Walter Gehring’s laboratory for the thirty years that followed. In the opening chapters of his book describing the discovery of the homeobox (Master Control Genes in Development and Evolution, Yale University Press 1998) Walter reminisces on those early years in Basel and on the challenges in cloning genes and establishing a molecular biology of Drosophila. In those days, labs had to generate all their reagents by themselves and purify the limited number of restriction enzymes that were needed for establishing recombinant DNA libraries — his lab residing in Switzerland, they were called ‘gene banks’. There was no obvious way of characterizing specific clones in the libraries other than reliance on RNAs that were sufficiently abundant that they could be isolated in quantities to use as probes for in situ hybridization on giant chromosomes. The initial successes of physically isolating Drosophila genes in his lab, therefore, involved highly expressed genes like those encoding 5S ribosomal RNA and heat shock proteins.

Walter Gehring’s success as an eminent scientist relied heavily on an astoundingly good group of postdoctoral fellows to push forward those analyses. His ability to attract young scientists trained in molecular genetics to his lab reflected one of his strengths as a scientist. He gave fascinating seminars that made you think that fundamental problems in developmental biology were tractable at the molecular level and that they were now being solved — or to be solved — in his lab. Part of this attraction was his belief that the solutions were simple, that discrete maternal determinants existed in the egg, and that ‘master control genes’, such as Antennapedia/Nasobemia operated in clear hierarchies that control cell fate.

For insiders working in the complex and somewhat esoteric areas of Drosophila developmental genetics, his presentations (and his enthusiasm for his own experimental results or the results of his collaborators) seemed sometimes oversimplified and naive. It may be fair to say that he never deeply appreciated what could be learned from sophisticated genetic analyses of embryonic development, or cell lineage studies on compartmentalization of imaginal discs. He once expressed skepticism dismissing all double mutant analyses, arguing that combining two defects in the same individual could never be informative about the underlying normal biology. He also had a hard time appreciating women’s contribution to science, arguing that there was ‘no female Einstein’ and women had strengths in other professions. On the other hand, his self-confident simplicity brought an underlying strength and power to his research program and provided an impetus and encouragement to his postdocs and students to attempt difficult experiments that caution would have argued against pursuing.

More importantly, however, it turned out that sometimes processes in nature are indeed as simple and exciting as Walter believed. The first important breakthrough followed the chromosomal walk to the Antennapedia gene performed by three postdocs in his lab. Not only did his much beloved gene encode a protein with the DNA binding
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Gehring’s group: A wall painting of Walter Gehring (seated) surrounded by his research group, shortly after his return to Switzerland. The painting was done by Eric Wieschaus (lower left) for the 1973 Biozentrum Fasnacht celebration. Erica Wenger Marquardt, Walter’s long-term and extremely loyal secretary, is recognizable in the upper left.

properties he had anticipated in his failed postdoctoral experiments, but it contained a region of homology shared with the other homeotic Drosophila ‘master control genes’ of the bithorax complex discovered by Ed Lewis and cloned in the laboratory of David Hogness. Most importantly, this region of homology, dubbed the ‘homeobox’, could be found in the genomes of a wide range of animals, including vertebrates and humans. In these organisms, as well as in Drosophila, transcription factors that possess the homeobox seem to play critical roles in establishing the basic body plan of the organism. The discovery of the homebox in Walter’s lab (and its simultaneous discovery by Matthew Scott working in Thom Kaufman’s lab in Indiana) enforced the idea that evolutionarily distant organisms might share common developmental pathways and common genetic circuits. This idea is now taken for granted in all current genomic approaches, and today it seems strange that it was completely unanticipated in 1980 at the beginning of the cloning era. The discovery of the homebox provided one of the best and most convincing examples of that homology and probably more than any other single observation transformed thinking in the field.

That genes might conserve DNA binding domains or specific biochemical activities is no longer surprising. Perhaps more remarkable was that those activities would be conserved in specific developmental pathways. One of the great mysteries that have puzzled evolutionary biologists since Darwin is the convergence of similar structures and functions in organisms that are only distantly related. A prime example has been the evolution of eyes with very distinct morphologies in flies and vertebrates. Evolutionary biologists had long assumed that light sensing organs had evolved separately and independently in the two lineages. If this were the case, one would expect the developmental pathways not to be conserved. The demonstration that both the Drosophila eyeless gene and its vertebrate homologue small eye could function as a master regulator, inducing eye development in whatever region of the fly it was misexpressed, was a major breakthrough for Walter’s lab. Like the discovery of the homebox itself, the result provided additional evidence for a common ground connecting all animal phyla.

Walter was a gregarious scientist who enjoyed meeting and discussing his latest results with others. He was a great orator who contributed much to public understanding of modern biology and evolution. He was also an inspiring teacher — he followed his mentor Hadorn as coauthor of a classic zoology textbook with Rüdiger Wehner. In his childhood, he was a bird watcher and naturalist — his master’s thesis was on bird navigation! He remained a great naturalist throughout his life and one of us (E.W.) fondly remembers bird watching with Walter in Cape Cod soon after he had joined the lab as a graduate student. In his later years, Walter spent much of his time in marine biological stations, where he also gave summer courses. He loved reunions with his ex-students and postdocs who organized splendid festivities for his birthdays. He will be missed.

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The Sixth Extinction: An Unnatural History
Elizabeth Kolbert
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There really are more than two kinds of people in this world. It’s just that in addition to the two common ones, the third class is rare. There are those of us for whom slinging a hammock between two trees, draping first a mosquito net over it, then a rain fly, is as close to a definition of paradise as imaginable. There are those for whom this would be cruel and unusual torture. And, then there is Elizabeth Kolbert, who might have remained one of the latter, but has the pluck to sling her hammock and write about it.

Walking through the forests of Panama, her guides point out the soldier ants, which leave their jaws in your legs after they’ve bitten. They look for, but do not find, the most venomous snakes, that “can really mess you up” and, eventually, the hammock site. “A slit in the bottom constituted the entryway, and … when I climbed into the thing, I felt as if I were lying in a coffin.” In this coffin, she has “vivid troubled dreams” of “bright yellow frogs”. Forest spirits do us — human actions are driving species to extinction at rates only seen five previous times in geological history.

Kolbert is brave in another sense. Her main title is the same as the book by distinguished science writer Roger Lewin and famous anthropologist Richard Leakey, published in 1996. Kolbert is a staff writer at The New Yorker, a popular US magazine, and brings an essayist’s approach to the topic. Indeed, her book is a set of thirteen essays, with a three-page introduction and no summarising thoughts.