Open questions

A forest of principles
Horace Barlow

I am astonished at Lewis Wolpert's claim that all the big principles in biology are understood — especially in developmental biology. If one knew all the principles then new facts would simply slot into their expected places, as they do in any well understood aspect of physics. But in all areas of biology bewildering new facts are discovered at an increasing rate. I frankly do not believe that Wolpert has a conceptual scheme where each new fact simply evokes an acquiescent nod of the head. Either he is goading us into protest or his 'principles' are very different from mine.

What can we expect of principles in biology? Consider 'the principle of quasi-optimal design.' There are physical limits that dictate the relative sizes of parts of different-sized animals. Thus, a mouse's eye is many times larger than an elephant eye scaled down in proportion to the size of the mouse: the latter would have a minute pupil giving appalling spatial resolution and admitting very little light. Similarly, the elephant's legs would break every time it stood up if they were simply the mouse's legs scaled up in size.

These 'design principles' are our minds' generalization from particular instances that have been embodied in genomes under the action of natural selection. We have successfully found a few such generalizations, but we emphatically do not understand all the physical limiting factors that have moulded the genomes of all species, and I have not even heard mention of limiting factors in development, although they must surely exist.

Now consider a problem in neuroscience. The neocortex of the brain is large in primates and huge in humans; comparative neuroanatomists have told us that it stores knowledge of the world, and if they are right, we can understand the selective advantage it gives us. Neurophysiologists, on the other hand, tell us how the neocortex represents sensory stimuli but say nothing about how this representation is analysed, stored, accessed or used. Only a fool could hold that no new principles might emerge from reconciling these two astonishingly different accounts.

I think my examples illustrate the general nature of biological principles. There are not just a few universal ones like the great conservation laws of physics. Instead, they form a forest, and quasi-optimal design is but one tree in it — or perhaps just a branch of the Tree of Adaptation. Wolpert might claim that adaptations are all examples of a single general principle which we already know, but this is unhelpful because we need to know what factor is limiting in each particular case: optics will not help you to understand the elephant's leg bones or neocortical size. If we did understand all the relevant limiting factors, we would be closer to knowing why a species has evolved to a certain average size, why the mass of its neocortex is a particular fraction of its body mass, and so on for many questions that we do not yet even know enough to ask. It is an absolutely safe bet that there are many new principles waiting to be found.

Mendel discovered both a whole range of new facts and the principle by which they could be understood, but few are so lucky nowadays. Thus, my request to the good fairy godmother of science would be "Please give me exact references to some facts that require new concepts for their understanding". I would add "Please pick facts pointing to concepts appropriate for my energies and abilities; I could not handle a tree of Darwinian or Mendelian size, but I would greatly enjoy some of the conceptual fruit still to be found in plenty out among the leafy branches of the Biological Forest of Principles".

Pedigree

The Morgan lineage
Guil Winchester

Intellectual pedigrees convey the longevity and continuity of scientific lineages. The *Drosophila* community founded by Thomas Hunt Morgan and the Columbia Fly Room is still flourishing after eighty-five years.

Figure 1

The pedigree is skewed to show how the *Drosophila* renaissance in the 1980s descends from the Columbia Fly Room. Descendants who founded schools in other organisms are also shown, but their 'heirs' are not (unless they move back into flies). Individuals are listed only once. Thus, interactions within labs can be deduced but not the spread of ideas and techniques via the movement of postdocs. The pedigree is divided vertically into filial generations and horizontally into sublineages. At the top left are the 'triumvirate' who 'invented' *Drosophilia* as a genetic organism, Morgan and his two graduate students Sturtevant and Bridges. All three moved to Caltech when Morgan founded the Division of Biology (1928), and the pink band contains Morgan's direct line, which formally descends through Sturtevant. 'F_2' graduate students are those selected by Sturtevant himself (*A History of Genetics*. New York: Harper and Row; 1965), plus Lindsley. Delbrück is also on Sturtevant's Caltech pedigree and illustrates the movement into 'lower' organisms in the 1930s–1940s, followed by the move back into flies in the 1960s–1970s. (Delbrück was a cofounder of the 'phage group; Benzer founded *Drosophila* neurogenetics.) The beige and yellow bands also descend from Columbia. Muller, a semi-detached member of the Fly Room, moved often and founded several schools; only his Texas and Edinburgh heirs are shown here. Stern was the most successful of the Fly Room postdocs: he and Hadorn (an amphibian embryologist who moved into flies via a postdoc with Stern) pioneered *Drosophila* developmental biology. In the lowest band are two Caltech postdocs: Dobzhansky founded a school of *Drosophila* population genetics at Columbia; Beadle 'invented' *Neurospora* as a tool for biochemical genetics and succeeded Morgan as head of Caltech's Division of Biology. Two of Beadle's heirs moved back into flies: Mitchell in the 1950s and Hogness in the 1960s. The Hogness laboratory pioneered *Drosophila* molecular biology and launched the *Drosophila* renaissance.