both depth and time. So they directly observe the evolution of both the expansion and compression waves with picosecond resolution.

The authors use a titanium:sapphire laser both to heat the test sample, and synchronously to produce the X-ray pulse (see Box 1). By use of a beamsplitter, a small part of the laser energy irradiates a GaAs wafer to produce the ultrasonic pressure pulse, while the rest is focused on a small spot of the copper wire to produce the X-rays. These picosecond X-rays are then diffracted from the GaAs crystal and recorded on a charge-coupled device. The exact timing of the X-ray diffraction from the GaAs can be altered by changing the optical path difference between the two parts of the beams. This allowed Rose-Petruck *et al.* to monitor the acoustic pulse for several hundred picoseconds after it was initiated. The acoustic waves caused by the ultrasonic pressure within the crystal are monitored by recording the change in the Bragg scattering angle owing to the change in the distances between the atoms. As the X-rays simultaneously penetrate regions of both compression and expansion, a complicated algorithm is used to extract the strain as a function of depth.

Further developments in time-resolved diffraction are on the horizon. Synchrotron radiation with a timescale of a few picoseconds has been used to monitor laser-irradiated semiconductors[10], and sub-picosecond X-ray pulses have been generated by Thomson scattering lasers from high-energy electron beams[7]. Such sources, only available at large facilities, complement the table-top K_α sources, as they can produce broadband X-radiation. But, whatever the relative merits of synchrotron versus laser-generated sources finally turn out to be, the work of Rose-Petruck *et al.*[8] clearly demonstrates the impressive potential of table-top picosecond X-ray sources, and brings us closer to the goal of watching, on femtosecond timescales, so-called 'molecular movies'. □

Justin Wark is in the Clarendon Laboratory, Department of Physics, University of Oxford, Parks Road, Oxford OX1 3PU, UK.
e-mail: justin.wark@physics.ox.ac.uk

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Olfaction

Good reception in fruitfly antennae

Yitzhak Pilpel and Doron Lancet

Insects have exquisite chemosensory faculties[1–3] — some can sense pheromones from several miles away. Yet although the genes for olfactory receptors in vertebrates[4,5] and the nematode worm *Caenorhabditis elegans*[6] have been known for years, their insect counterparts have remained elusive. Now, reports in *Neuron*[7] and *Cell*[8] describe the identification of genes for olfactory receptors in the fruitfly *Drosophila melanogaster*. These genes encode membrane receptor proteins that probably mediate odorant recognition in the fly.

The discovery of *Drosophila* olfactory receptor genes was possible largely due to the availability, in databases, of genomic DNA sequences. To find these genes, Clyne *et al.*[7] initially used a pure *in silico* approach. They assumed that *Drosophila* olfactory receptors would be structurally similar to the other known olfactory receptor genes. So, the authors identified two candidate genes from databases with an algorithm based on seeking their potential to code for proteins with multiple transmembrane segments. Vosshall *et al.*[8] first identified an olfactory-specific rare messenger RNA (as befits a protein expected to be expressed in only a small subset of sensory neurons). Both groups then found further transmembrane homologues by searching the archives of the *Drosophila* genome project and they confirmed that, as expected, the dozen or so candidate genes are specifically expressed in sub-populations of cells within the fly olfactory organs — the antennae and maxillary palps.

On statistical grounds, the new studies indicate that between 100 and 200 genes may code for the *Drosophila* olfactory receptors. This is far fewer than the estimated 500–1,000 genes active in many vertebrates, and even in the lowly *C. elegans*. On the other hand, the fruitfly may have a few dozen chemosensory cell types (compared with just 14 in the nematode), which converge on almost 50 vertebrate-like synaptic targets known as glomeruli[2].

Drosophila also seems to be the most ancient creature in which olfactory receptor genes are clonally excluded — that is, just one or a few genes are expressed in each of the sensory cells (Fig. 1, overleaf)[7,8]. This is an important feature if each odorant is to be accurately represented across the sensory neuronal 'activation vector' (that is, the firing frequency input from different types of

100 YEARS AGO

It is interesting to note how the gradual discovery of the attendants of the various planets has influenced the compounding of the "laws" which from time to time have been found to approximately represent the positions of these bodies in the solar system. From the first discovery of Jupiter's four satellites by Galileo in 1610 to Huyghens, Cassini, and Sir W. Herschel, no regular relationship was perceived. When, however, in August 1877, Prof. Asaph Hall discovered the two moons of Mars, Deimos and Phobos … it was seen that all the then known satellites were grouped in a geometrical progression, reckoning outwards from the Earth. Thus the Earth had one, Mars two, Jupiter four and Saturn eight. This seeming regularity was broken by the discovery on September 9, 1892, of a fifth satellite to Jupiter … . This last discovery of a ninth satellite for Saturn will furnish a reason for a new series being formed, as counting from the Earth outward from the Sun, the numbers of satellites to the planets Earth, Mars, Jupiter and Saturn are now 1, 2, 5 and 9 respectively, and these numbers are very nearly proportional to the distances of those planets from the Sun.
From *Nature* 23 March 1899.

50 YEARS AGO

Much of the published data regarding the mode of action of penicillin is necessarily concerned with secondary effects on bacteria, for example, rate of killing under different conditions, morphological changes, etc. By use of radioactive penicillin, it should be possible to find out directly something of the nature of the primary reaction between penicillin and the cell. Penicillin is taken up by all bacteria in amounts which increase with penicillin concentration … . There is, in fact, a direct correlation between the sensitivity of an organism and the amount of penicillin attached to it. … However, if growth is halted by cooling, or if the cells are already dead, there is still a rapid but smaller uptake. … Whatever the nature of the primary site of penicillin action, it is clear from this and other work that rapid growth exposes more centres in the bacteria with which the penicillin can react. The combination must either be by unusually strong adsorptive or by chemical forces.
From *Nature* 26 March 1949.

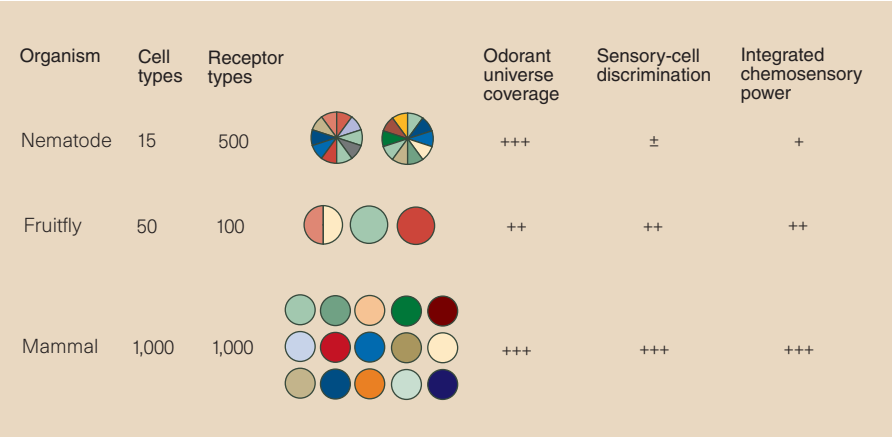

Figure 1 **Evolution of olfactory cells and receptor proteins. Nematodes and mammals have similar numbers of chemosensory receptor types[4,6], so they should detect the same (large) number of odorants with comparable sensitivities[13]. Because, in the nematode, sensory cells each bear many different types of receptor, individual cells may show poorer discrimination among odours. But mammals seem to have complete clonal exclusion — each sensory cell expresses only one type of receptor, giving the best possible discrimination at the level of single neurons. The fruitfly may represent an intermediate evolutionary step; the number of cell types has increased modestly, but the sensory neurons have gone most of the way towards clonal exclusion. This means that, although its olfactory receptor repertoire is smaller, it is much better than the nematode at discriminating odours. Additional gene-repertoire enhancement is mainly what is needed to attain the olfactory power of mammals.**

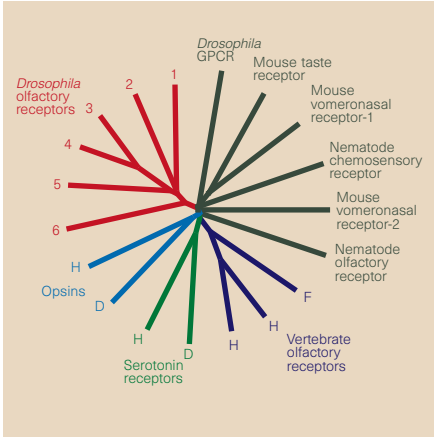

Figure 2 **Dendrogram analysis for the protein sequences of chemosensory receptors and G-protein-coupled receptors. Included are six of the *Drosophila* olfactory receptors discovered by Clyne *et al.*[7] and Vosshall *et al.*[8]. Although opsins and serotonin receptors are clear cases of human–*Drosophila* orthology, the *Drosophila* olfactory receptors are almost unrelated to their vertebrate counterparts. H, human; F, fish; D, *Drosophila*; GPCR, the G-protein-coupled (Frizzled-like) receptor.**

cell, used for integration of signals in the central nervous system)[2,4]. The new studies even shed light on the mechanisms by which such cellular exclusion is controlled. Vosshall *et al.*[8] suggest that a region 3 kilobases upstream of an olfactory receptor gene is involved, and Clyne *et al.*[7] implicate a transcription factor[9] called Acj6. In this respect, perhaps studies of the potentially simpler insect mechanisms will help us to work out how expression of olfactory receptor genes is controlled in higher organisms.

Could *Drosophila* and other insects have been the first to evolve the neuronal-integration device that vertebrates subsequently came to have[2]? If so, perhaps insects temporarily sacrificed the number of olfactory receptor genes so that they could evolve the elaborate cell-biological mechanisms needed to process chemosensory information more accurately (Fig. 1). Only later, with the advent of the vertebrate olfactory system, could both high receptor count and sophisticated neuronal wiring exist together. Interestingly, a dendrogram analysis (Fig. 2), which shows the relationship between different genes and organisms, may place the new *Drosophila* olfactory receptor genes, as well as some nematode chemosensory receptors, slightly nearer to receptor genes[10,11] expressed in a vertebrate 'accessory olfactory pathway' (the vomeronasal organ, and the recently discovered[12] vertebrate taste receptors). So, the main olfactory system in vertebrates has emerged with a separate set of chemoreceptive genes, more akin to visual photoreceptors and neurotransmitter receptors, which may have taken over an existing clonal-exclusion machinery.

The *Drosophila* olfactory receptor genes are unique, and there are no obvious counterparts with similar sequences in other species. In fact, their sequence is so different from other chemosensory receptors that one could even suspect a transduction mechanism[1] other than the usual coupling to guanine-nucleotide-binding (G) proteins[4,5]. In this, olfaction is unlike many other functional pathways, where clear structural and functional relationships can be traced across 500 million years of evolution (Fig. 2).

One possible reason for this is that fruitflies might have an idiosyncratic odour world[8]. To find out whether this is so, we could compare the olfactory-receptor sequences in insects with different behaviours and habitats. An alternative explanation — which is more consistent with studies that indicate nothing special about insect odorants[3] — is that chemosensory repertoires evolved with a free rein, perhaps under balancing selection (which is known to generate diversity for diversity's sake). Just as in a combinatorial library, an olfactory repertoire could be fully functional as long as it is large and eclectic enough[13]. This could lead to the appearance of disparate chemosensory proteins in different phyla.

Some characteristics of invertebrate olfactory receptor genes contrast with those of the vertebrate receptors. For example, whereas the *Drosophila* and *C. elegans* genes are interrupted by introns within the protein-coding sequences, the coding regions of vertebrate olfactory receptor genes are intronless. This curious phenomenon suggests that the loss of introns is, in this case, a later evolutionary adaptation. Because many other seven-transmembrane-domain receptors are also intronless, the phenomenon could reflect a general characteristic of this type of transduction protein[14]. However, the mechanisms leading to the loss of introns in olfactory-receptor genes may have had more to do with the need for extensive gene duplication[5,14] to allow the evolution of fully fledged vertebrate olfactory repertoires.

In less than a year the *Drosophila* genome will probably be fully sequenced, leading to a complete knowledge of the fruitfly 'olfactory sub-genome'. By unravelling the olfactory-receptor genes in one of the most coveted model organisms, replete with powerful genetic and developmental tools, we will surely be able to solve many of the questions about how we, and other species, perceive the chemical universe that surrounds us. □

Yitzhak Pilpel and Doron Lancet are in the Department of Molecular Genetics and the Genome Center, Weizmann Institute of Science, 76100 Rehovot, Israel.
e-mails: bnpilpel@membran1.weizmann.ac.il
bmlancet@weizmann.weizmann.ac.il

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