# Images at the blind spot

SIR — Ramachandran and Gregory[1] explored the intriguing question of how we "fill in"[2] that part of a scene which is not sampled by the visual system — one example is the blind spot, discovered by Mariotte in 1660. Helmholtz[3] reviewed the early literature but was unable to put forward a satisfactory theory.

We have devised a new method to investigate the response to images on and near the blind spot. Using a desktop computer, contiguous black squares each subtending 20' at the eye were successively displayed on the screen, forming a horizontal line which gradually extended from one side of the screen to the other at 2° per second. A fixation point was provided.

Initially, one sees clearly the line starting at one side of the screen and lengthening towards the centre (see figure). When it arrives at the edge of the blind spot, all movement ceases and the line appears to maintain its position and length; despite the fact that squares continue to be added and their images cover more and more of the blind spot. Eventually, when a square exits the other edge of the blind spot, it is seen as a continuation of the original line which had stopped. The line is suddenly seen to lengthen once more. The duration for
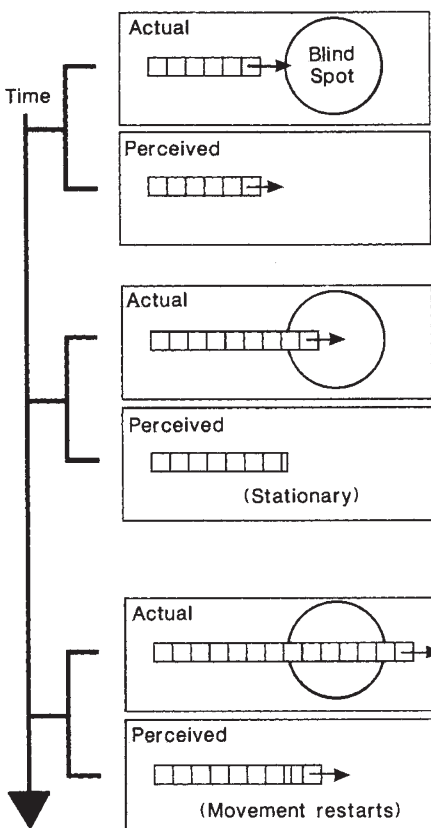
Actual and perceived movement at three successive instants.

which the movement is stopped equals the time required for the squares to move a distance equal to the diameter of the blind spot, as measured by conventional means (5°).

In the second experiment, two stimuli were used, each identical to those in the first experiment but with the lines separated vertically so that the image of one passed above (or below) the optic nerve head. The appearances of each of the two resulting lines were dramatically different. The line that traversed the blind spot was seen to be shorter. For example, if the total subtense of the lines were 10°, the line traversing the blind spot was seen to be shorter by 5°, half the length of the comparison line that missed the blind spot. These effects are so pronounced that they are readily and instantly perceived by the most inexperienced of subjects, presumably because they involve relative movement as opposed to more conventional, static demonstrations. Our technique may be diagnostically valuable, particularly as the movement would make the patient's task of reporting much easier. A copy of the program discussed above is available from us.

P. R. ANDREWS
F. W. CAMPBELL

Physiological Laboratory,
University of Cambridge,
Downing St, Cambridge CB2 3EG, UK

1. Ramachandran, V. S. & Gregory, R. L. Nature 350, 699–702 (1991).
2. Rudolf, N. D. de M. & Wilson, M. E. King's College Hospital Gazette 37, 1 (1958).
3. Helmholtz, H. Treatise on Physiological Optics Vol II (ed. Southall, J. P. C.) 170–220 (Dover, New York, 1962).

Muller's ratchet and flu virus

SIR — According to Chao[1], the fitness of RNA viruses can be decreased by Muller's ratchet. Chao's findings in a bacteriophage system are also applicable to influenza virus populations.

The ratchet operates in viral populations which undergo periodic bottlenecks. Following infection with influenza virus, for example, individuals develop a humoral immune response which protects them from reinfection with the same virus. After an influenza virus strain has circulated extensively, most of the world's human population becomes immune to reinfection[2]. Thus the number of susceptible individuals to support influenza virus replication is drastically reduced and with it the pool of human influenza virus genes: the immune response imposes the bottleneck. Eventually, influenza virus genomes containing critical mutations on the genes for the surface glycoproteins which allow them to evade the immune response, arise. These viruses, usually one or a few

particles, are able to reinfect previously immune individuals and act as propagules. At this point, the human influenza virus population escapes the bottleneck and the progeny of one or a few genomes will become the prevalent virus population, as found by Chao.

Nucleotide sequence and phylogenetic analyses of each of the eight RNA segments of the genome of flu virus isolated from humans and animals during the past 40 years have led to the construction of evolutionary trees of the influenza virus genes[3,4]. Detailed analyses of the evolution of these genes reveal that the selective pressure of the immune response on haemagglutinin (HA) and neuraminidase (NA) genes results in the fixation of random mutations in these genes and in other viral genome segments, such as segment 8 (encoding nonstructural proteins NS1 and NS2) or segment 1 (encoding basic polymerase PB2)[3,4]. The genes encoding PB2, NS and nucleoprotein (NP) of human influenza viruses have accumulated many silent and nonsilent mutations in their genomes as a consequence of population bottlenecks imposed by immune selection. Decreased fitness of the derived (recent) influenza genomes would be predicted if Muller's ratchet applied to this human influenza virus–host system.

The re-emergence of an ancestral fossil genome ('Russian' strains, similar in nucleotide sequence to A/Fort Warren/ 50, dating from 1950) in the human population in 1977 offers the possibility of testing this prediction. After the reappearance of this fossil there was ample opportunity for reassortment of genome segments. Viruses such as A/California/ 78 and A/Kiev/59/79, which have genomes consisting of a mixture of genes from the circulating viruses and the reintroduced fossil virus, were isolated from the human population during two consecutive seasons. Were Muller's ratchet applicable, the fossil influenza virus genome segments reintroduced in 1977 would have displaced by reassortment the more derived and less fit circulating gene segments (evolved from the 1950 virus ancestor). Recent isolates of influenza virus from humans do indeed have the derived NS, NP and PB2 genes with cumulative mutations and not the fossil genes, suggesting equal or greater fitness in the derived genes. Thus the reintroduced virus is still in circulation but it did not displace the previously circulating virus lineages.

These findings can be reconciled with those of Chao in the bacteriophage sys-

1. Chao, L. Nature 348, 454 (1990).
2. Couch, R. B. & Kasel, J. A. A. Rev. Microbiol. 37, 529–549 (1983).
3. Buonagurio, D. A., Nakada, S., Parvin, J. D., Krystal, M., Palese, P. & Fitch. W. M. Science 232, 980–982 (1986).
4. Gorman, O. T., Donis, R. O., Kawaoka, Y. & Webster, R. G. J. Virol. 64, 4893–4902 (1990).