million years ago, the SINE insertion event could have been considerably earlier. The only rat A_β nucleotide sequence available[7] should reveal whether the sequence motifs characteristic of the allelic groups of the genus *Mus* exist in a species whose time of divergence from the mouse must have been at least 10 million years ago (see figure). It is very striking how at almost every position (26/30) at which grouping according to McConnell *et al.* is defined, the rat gene shows one or other of the defining nucleotides. Admittedly, similar information is not available from another rat A_β allele, but it is tempting to propose that many of these substitutions are ancient, and will be found to have antedated rat–mouse divergence.

One of the biggest problems in long-range evolutionary analysis of MHC sequence variation follows from the instability of the genomic organization of both class I and class II genes, with extensive duplication and deletion. General family relationships are preserved, as between human HLA *DQ* and mouse *H-2 A* genes, but there is no simple one-to-one correspondence between the human and mouse genes within the family. It is therefore impossible to follow allelic sequence variation with any assurance over such time intervals. In the rat, however, the central regions of the class II system seem to be orthologous to those of mouse, containing exactly the same genes in the same orientation in a simple one-to-one correspondence[8]. There is therefore no objection to extending the analysis[1] to the rat.

The selective forces responsible for MHC gene polymorphism are not fully understood, but probably follow from defensive strategies available to rapidly evolving pathogens. To avoid T-cell recognition and immunity, potentially antigenic peptides of pathogen origin either must fail to bind to MHC molecules, or in doing so must mimic self structures to which the host is tolerant. In either case, possession of two different allelic forms of MHC molecule improves the host's chances of mounting a successful immune response. Conventional heterozygous advantage is therefore probably involved. Second, pathogen evolution will be guided by the need to subvert abundant allelic forms, so that rare alleles will tend to enjoy a selective advantage. Frequency-dependent selection will therefore favour multiple alleles with low individual allelic frequencies, and hence a high degree of heterozygosity. The data presented by McConnell *et al.* suggest that at least a part of the polymorphic variation available in existing populations of mouse is relatively ancient, though this is probably more true of the substitutions themselves than of the array of substitutions that make up each modern allele, at least as far as the $A_{\beta 1}$ exon is concerned. The pattern of allelic evolution in the MHC emerging from this and other studies is consistent with the idea that several processes with different timescales are at work. There is no reason to invoke point hypermutation targeted to MHC genes.

However, new coding substitutions in regions of the molecule associated with peptide binding seem to be under intense selection. The low allelic frequencies suggest that while such new substitutions may enter the population rapidly, they rarely completely replace existing alleles. Rather, they join the very large pool of alleles already present and stay fluctuating in frequency in the population for several million years. During this time, allelic point mutations are reshuffled with others by recombinational mechanisms to generate functionally new alleles which are themselves subject to further rounds of pathogen-dependent selection. Perhaps peptide-binding domains of MHC molecules are favoured targets for reshuffling processes, and other parts of the genes evolve fairly conventionally. Only by further fine analysis of the structure of MHC sequence polymorphism within and between species will the relative importance of these distinct mechanisms become clear. □

	$A_{\beta 1}$	$A_{\beta 2}$
Group 1	A.GG. GAG. A.C. GC. CCGG. GATC. G.C/G	C. G.A.A.AT. A.C. T. A
Group 2	A.GG. GAG. G.T. AG. ---T. C---. G.G	T. A.C. G.GG. G.C. T. A
Group 3	C.CC. TTC. A.T. AG. ---T. C---. A.A	T. A.C. G.GG. G.T. C. C
Rat	A.GG. CTG. G.C. GC. AAGG. GATC. A.A	C. A.C. G.GG. G.C. A.C

Diagnostic nucleotides defining the three groups of A_β alleles of McConnell *et al.* for the $A_{\beta 1}$ and $A_{\beta 2}$ domains, compared with the one available A_β sequence for the rat[7]. Only the group-diagnostic nucleotides are shown and other sequence is indicated by dots. Dashes indicate deleted nucleotides. Underlined nucleotides show identity with the rat sequence at these positions. The segmental organization of diversity is apparent in group 2, which begins with six bases from group 1, and thereafter follows group 3. Similarly, the rat sequence stays with group 1 for most of the $A_{\beta 1}$ domain, but follows group 3 thereafter.

1. McConnell, T. J., Talbot, W.S., McIndoe, R.A. & Wakeland, E.K. *Nature* **332**, 651–654 (1988).
2. Klein, J. *Hum. Immun.* **19**, 155–162 (1987).
3. Germain, R.N. *Nature* **322**, 687–689 (1986).
4. Bjorkman, P.J. *et al. Nature* **329**, 506–518 (1987).
5. Nathenson, S.G. *et al. A. Rev. Immun.* **4**, 471–502 (1986).
6. Parham, P. *et al. Proc. natn. Acad. Sci. U.S.A.* (in the press).
7. Eccles, E.J. & McMaster, W.R. *Immunogenetics* **22**, 653–663 (1985).
8. Diamond, A.G. *et al. Transplant. Proc.* **17**, 1808–1811 (1985).

Jonathan C. Howard is in the Department of Immunology at the AFRC Institute of Animal Physiology and Genetics, Babraham, Cambridge CB2 4AT, UK.

Daedalus

Unspoken words

MACHINE-translation of speech into written text is still defeated, in all but the simplest cases, by the variety, subtlety and rapid variation of human speech-sounds. So Daedalus is devising a speech-writing system that ignores sound altogether. Instead, it follows the speech-mechanism that makes the sound. In effect, it is the ultimate in lip-reading.

Intrepid DREADCO volunteers are gargling with magnetic fluids and applying red-iron-oxide magnetic lipstick, so that the speech-movements of their coated lips, tongue and mouth can be followed by a web of external pick-up coils. Less invasively, electrodes taped to their faces are recording the changing distributed resistances and myoelectric potentials of their speech; even non-contact electrodes can register useful changes of distributed capacitance.

The output gathered by these methods is logically 'upstream' of the speaker's sound-output, and closely linked to his internal verbal code. So it should be much easier to decode back into words — just as it would be easier to reconstruct the music of a piano by following the key movements rather than listening to the sound. With luck, a few key facial parameters will suffice to define a speech-state uniquely, and DREADCO's Speakwrite® need only record these. The first commercial model will probably feature an electroded mask held close to the speaker's face; but Daedalus hopes ultimately to devise some form of radio-denture or radio-toothbrace to monitor the key parameters from inside the mouth, and transmit them to the interpreter/word-processor unit nearby.

Thus the irksome barrier between speech and writing will be broken down: intermediaries like secretaries and keyboards will become redundant. The author or executive will talk directly to his Speakwrite. The text coming up on the screen will doubtless contain mistakes, but these will easily be rectified by coded commands, the verbal equivalents of keyboard corrections. As a telephone-cum-telex machine, it will enable speech at one end to emerge as text at the other. And, being independent of sound, it will do its work in the most impossible sonic conditions. It will faithfully record the whispered or merely mouthed speech of the clandestine eavesdropper or Trappist novelist; it will accept the words of the tank-commander or rolling-mill manager against the most deafening clangour; it will flawlessly interpret the quacking falsetto of the deep-sea diver in his helium-oxygen atmosphere, or the thick croaking of the sufferer with a really heavy cold. Even the deaf and dumb will be able to converse by Speakwrite.

David Jones