# HIV in infected lymph nodes

SIR — To answer questions raised by Duesberg[1], and in a separate and scientific sense by Phillips *et al.*[2], concerning the quantities of HIV RNA (detected by *in situ* hybridization) contained in the germinal centres of lymph nodes of HIV-infected individuals, we have constructed a test object containing a known number of HIV virus particles in a fibrin clot[3]. This sample can be processed in a manner identical to infected tissue specimens and examined histologically after *in situ* hybridization using a $^{33}$P-labelled HIV antisense riboprobe cocktail representing about 9 kilobases of the HIV-1 genome[4]. An equivalent-sense probe control is used to subtract background from consecutive sections of the test object and of the tissues. Tissue specimens are digested with protease to remove proteins adherent to the viral particles[5]. The amounts of hybridization are detected by phosphorimaging the microscope slides in a Fuji BAS 2000 instrument.

Calculations show the test object to contain 15,450 viral particles per mm$^2$ of a 6-μm section. Based on a comparison of 1-mm$^2$ (6,000-mm$^3$) portions of the test object with equal areas of lymph-node germinal centres showing maximum intensity, we estimate the number of viral particles in a germinal centre to be as much as $2.48 \times 10^4$ particles per mm$^2$. Because about 20% of the volume of lymph nodes is occupied by germinal centres in HIV-infected individuals (C.H.F., unpublished data), an entire lymph node may contain of the order of $1.2 \times 10^9$ viral particles per cm$^3$. The amount of viral RNA appears to remain relatively constant in the germinal centres of lymphoid tissues in sequential biopsies. We have examined more than 300 tissues from individuals who had been infected for different periods of time (including gut, spleen and even lung when lymphoid aggregates occur there), which range from the time antibodies develop against HIV until up to 8 years after infection or until loss of germinal centres in the late stages of AIDS. A similar circumstance occurs in other primates infected with SIV.

In reply to questions regarding the infectious nature of such viruses, we refer readers to a series of relevant papers by the late Albert Sabin[6], in which he reported experiments showing that viruses that had been reacted with antibodies retain their infectivity in tissues. It seems reasonable to us that CD4-expressing T lymphocytes become infected following collision with stored, protein-cloaked virus, as the cells traffic through lymphoid germinal centres. There may also be loss of CD4 expression when infected T cells express HIV. Projected over years, the rate of T-cell replacement falls behind their loss and, combined with alterations of cell populations and the developmental microenvironment of the germinal centre arising from the infection, the balance of both structure and function in the immune system is catastrophically altered. We believe that the protein-cloaked virus in germinal centres, combined with some element of follicular dendritic cell function[7] and T-cell kinetics, is the explanation for the extremely slow but inexorable progression of the primate lentiviral diseases.

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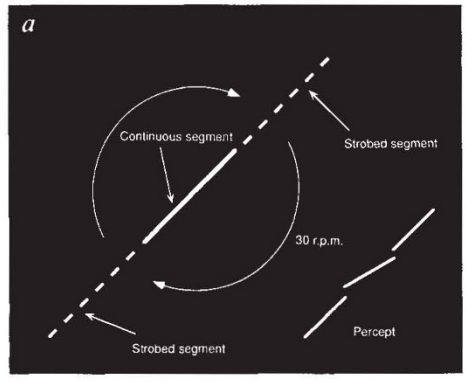
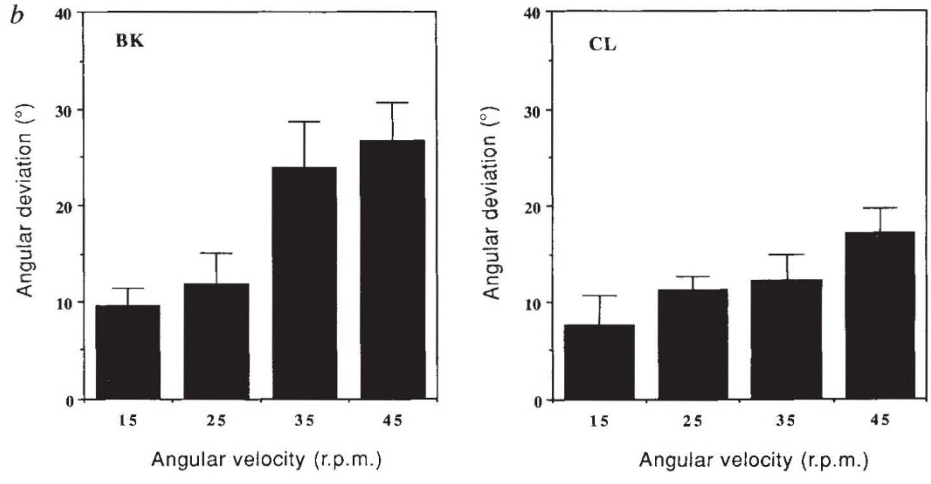
# Motion extrapolation in catching

SIR — Many studies investigate how observers might compensate for the latency due to bodily action while executing behaviours such as catching a ball. But success in such interceptive behaviour depends on the observer having accurate information about the ball's initial location. This raises a question that has received surprisingly little attention. How does the visual system compensate for the delay in the transmission of motion information from photoreceptors to 'higher' visual areas of the brain? The problem is serious because the typically estimated delay ($\tau$) of about 100 ms (ref. 1) would cause an object moving at 30 m.p.h. to appear retarded by 4.4 feet in its trajectory!

An effect first observed by MacKay[2] and later rediscovered in our laboratory[3] in the following form, suggests an answer. A single white line is rotated against a black background (see *a* in the figure). The line consists of one continuously illuminated segment and two strobed segments. Observers report a compelling




*a*, The stimulus was a single physical slit (3.9° long) rotating continuously at 30 r.p.m. against a dark background. The central 1.3° of the slit was continuously illuminated (solid line) and the two outer 1.3° segments were strobed (dashed lines) for 5 ms. Ten observers (six naive) reported a compelling spatial lag of the strobed segments (percept). *b*, The spatial lag increased as a function of the angular velocity of the slit. This lag was measured by having two observers (BK and CL) turn a disk to rotate the strobed segments relative to the continuous segment until they appeared to neither lag nor lead.