Existence of syphilis in a Pleistocene bear

SIR—In questioning our claim[1] to have identified signs of trepanemal disease in a Pleistocene bear, E. J. Neiburger[2] seems to be both unwilling to give credit to the power of modern techniques and to be unaware of some published accounts of the disease.

The extensive periosteal reaction and skeletal distribution of lesions in *Arctodus simus* are in fact characteristic of what has been reported in treponemal disease[3] and are indistinguishable from diseased treponemal specimens I have examined in medical museums. These differ from the more typically pauci-ostotic, non-spiculated involvement of tuberculosis and other chronic granulomatous diseases[4].

Spinal involvement in treponemal disease is frequent and is considered appropriate as the site for diagnostic bone biopsy[5]. The non-neuropathic spinal lesions in treponemal disease are characteristically lytic anteriorly, involving two to three adjacent vertebrae with hyperostosis and longitudinal ligament calcification[6], as in *Arctodus*.

Neiburger's suggestion that such lytic disease (sparing posterior structures) is a "unique finding to tuberculosis" is odd. Malignant processes tend to disregard tissue planes and cause posterior element destruction, not treponemal disease[7]. Nor is posterior destruction produced by invading organisms which, in producing gumma, typically affect the anterior components[6].

Neiberger seems to share the popular misconception that treponemal infection has not been found in non-primates, contrary to the evidence from hamsters and rabbits[8]. It is also found in various primates. Determining its presence in other populations would be of value in analysing epidemiological significance. The fact that immunological techniques identified the antigen is not surprising, as antigen survival for more than 100 million years has been documented[9,10]. The presence of antigen only in the walls of the gummas, together with its absence in uninvolved areas of the skeleton or in control materials, makes it unlikely that the antigen is a contaminant from handlers of the specimen.

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how to get from this underlying symmetry to an observed asymmetry, not what kind of formalism (chaos and the Brussels school, or coarse graining) is best at expressing such an asymmetry. The Brussels school seems to have simply replaced the asymmetric assumptions Boltzmann was so criticized for using in the derivation of his differential equation (the H-theorem) with a new set of asymmetric assumptions allowing them to derive their differential equation. The shortcoming in the approach is the same: you cannot have an asymmetry serve as the starting point of your analysis of macroscopic physics when there is no such asymmetry in microscopic physics.

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Insertional mutagenesis and breast carcinoma

SIR—Morse *et al.* recently described an interesting case of LINE-1 sequence insertion into the second intron of the c-*myc* oncogene in a human breast carcinoma[1]. Repetitive sequences such as the LINE elements are found in multiple copies in the mammalian genome and some of them are capable of transposition[2].

Several reports have documented the insertion of LINE sequences in various gene loci[2]. Because the activation of the c-*myc* oncogene may be involved in the pathogenesis of breast neoplasia[3,4], it is important to unravel the functional effects of the LINE sequence insertion in the c-*myc* gene in this example. Neither analysis of c-*myc* expression, nor transfection experiments were described in the paper, and the biological significance of c-*myc* insertional mutagenesis is therefore not clear. Morse and collaborators also failed to mention that this was not the first report of LINE sequence insertion in the c-*myc* locus.

We have described LINE insertion 5' to the c-*myc* gene in the canine transmissible venereal tumour[5,6]. Another example of LINE integration in the c-*myc* locus was recently described in a rat immunocytoma[7]. The discovery of three cases of insertional mutagenesis at the c-*myc* locus by a LINE sequence in various tumours in different species may suggest that these events are not random. The insertion of transposable elements into preferred genome loci is well documented in prokaryotes and similar 'regional specificity' also exists in eukaryotic systems[8]. Some oncogene loci may be preferred integration sites for certain repetitive movable genetic elements and this could result in oncogene deregulation and activation. In the case of the endogenous retroviral-like intra-

Chaos of the Brussels School may not be irreversible

SIR—In addition to the criticism already expressed in the conclusion of Peter Coveney's review article of the Brussels School (*Nature* 333, 409; 1988) I would like to add another. The essence of this criticism is that all the interesting mathematics of the Brussels school is besides the point, since the school has not explained why the underlying physics should imply any of this interesting mathematics in the first place. In particular, no argument is presented to explain why the underlying (time-symmetric) physics should imply the (overtly time-asymmetric) equations which serve as the starting point for the Brussels school.

It is all very well to talk of systems evolving chaotically into the future, but the real question is why systems cannot then also evolve in the same chaotic fashion into the past (in which case arguments based on chaotic evolution would presumably predict no time variation at all). It is important to note that this problem cannot be resolved by pleading initial conditions — the difficulty lies in getting an asymmetric differential equation in the first place, not in evaluating its consequences.

There are two stringent requirements which must be met if the problem of macroscopic time-asymmetry is to be solved. The first is that the underlying mathematics of the formalism must evolve things backwards in time in the same way that it evolves things forwards in time, because otherwise the analysis is being rigged in advance. Failure to pass this requirement is the shortcoming of the usual thermodynamic 'proof' of the Second Law using Carnot's laws on the maximal efficiency of heat engines. Given that the formalism does evolve things in the same manner in both temporal directions, the second requirement is to show why nature in fact chooses one direction in time over the other. (The trick in passing this second requirement is to do so without invoking an asymmetric argument, thereby dropping you back into the jaws of the first requirement.) Unfortunately, the Brussels school seems to never reach the second requirement because they overtly violate the first requirement.

Trajectories or distributions, single particles or many particles, the underlying physics must still be symmetric. The problem of macroscopic irreversibility is