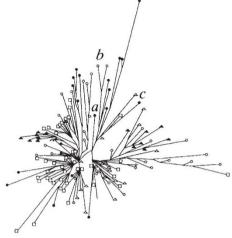
SCIENTIFIC CORRESPONDENCE

to make them all the same length. This tends to mask inequalities in rates of substitution along the different branches. More subtly, to keep all the horizontal branches parallel, it is necessary to introduce vertical lines of various lengths. These lines, which correspond to no feature of the data, impart an artificial air of organization to the tree - the bushier the main branches of the tree.



Starburst plot of the data of Cann et al.1. a, Position of the Ione African bushman in the sample: b, the anomalous Asian members of the 'African' branch; c, position of an Australian aboriginal near the same branch. Note another aboriginal at the base of the branch. Black circles, African ancestry; open squares, European: open triangles, Australian Aborigine; closed triangles, New Guinea; open circles, Asian.

the longer the vertical lines must be to separate them.

The effect of these distortions can be removed by redrawing the original data of Cann et al. so as to preserve the varying lengths of the branches and to avoid introducing any arbitrary separations between them (see figure). The result is an unrooted tree like a starburst, with the viewer looking back in time, and with the origin of the tree somewhere in the middle of the starburst. The tree shown is one of the many trees that are shorter than the original one, trees that can easily be generated by PAUP⁸, and the 'African' branch is near 12 o'clock. In this typical tree, the branch includes Asians, with one European and two Aborigines very close to it. When the data are looked at in this way, the impossibility of positioning the tree's origin with any certainty can easily be understood.

The starburst plot emphasizes the remarkable overdispersal of the data, with very unequal branch lengths and members of most groups scattered from the centre of the starburst to its periphery. These data are not alone in showing this overdispersed character, which has bedeviled the construction of phylogenetic trees from the beginning⁹. The impor-

tant question now becomes whether it is possible, by some combination of population subdivision, migration and fluctuating population sizes, to generate such a tree assuming a constant rate of neutral mutations, or whether it is necessarv to postulate fluctuating mutation rates and/or selective pressures in the various branches.

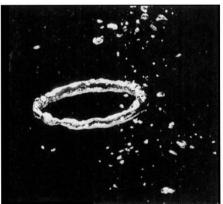
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Toroidal bubbles

SIR - The discussion about toroidal air bubbles by Daedalus¹ and Spisak² prompts me to mention our exhibit called "Friendship Acrobatic Troupe" by artist-in-residence Carl Cheng, in which a series of toroidal bubbles are formed in a 4-foot-deep transparent water tank through the actuation of a valved air jet. These toroidal bubbles float to the surface in an almost perfect ring. Smaller, detached bubbles clearly show the rota-



Toroidal air bubble.

tional flow of the liquid around the outside of the air ring. The toroidal rings are remarkably stable as they ascend up the tank (see figure). The bubbles are particularly beautiful because of the silver reflection produced by the light, which is incident directly from above and reflects due to total internal reflection.

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Alzheimer's – a correction

SIR - Lucotte and colleagues reported in Scientific Correspondence¹ the occurrence of a mutation (valine for isoleucine) in the β -amyloid precursor protein (APP) in a family in which both dementia and congophilic angiopathy occurs. G. A. and A. D. were responsible for the clinical assessment, DNA collection and neuropathological assessment of individuals from this family.

We have now carried out a further analysis of the APP gene. We used a BclI digest of the amplified product of exon 17 as a method for screening for the mutation². Despite the fact that we could detect the mutation in positive controls, BclI failed to digest any samples from this family. Therefore, we sequenced exons 16 and 17 of the amplified product, which revealed these exons to be of normal sequence in this family. Thus we regard the report by Lucotte and colleagues of the mutation in this family to be unreliable.

The valine to isoleucine mutation in exon 17 of the APP gene has been reported in six other families with Alzheimer's disease²⁻⁴; in these families its presence has been confirmed by direct sequencing. Further, two other mutations in the same amino acid have been reported^{5,6}. Thus, we are confident that mutations to this amino acid can cause Alzheimer's disease. We recommend that the occurrence of all mutations should be confirmed by direct sequencing.

The range of the phenotype of the mutation in exon 17 remains to be precisely delineated. Clearly, however, the age of onset of the disease is a variable feature (about 48 to about 60 years) as is the occurrence of Lewy bodies². So far, no patients in which this mutation has been confirmed have more than modest congophilic angiopathy.

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