hierarchy[16], in which many structures make connections with much higher or lower areas. These level-spanning connections contribute to the NMDS structure, but form a pattern that is not accommodated by the seriation method, so elevating the circuit length. Despite these difficulties, we optimized circuit length explicitly with simulated annealing and found an ordering with shortest circuit length of 196. There certainly is serial order in the data: the probability that the visual circuit falls in the distribution of random circuits is vanishingly small ($p < 10^{-49}$), and the data are more strongly serial than most empirical datasets in Archeology that are accepted as (serially ordered). Statistical comparison of the arrangement of areas in the optimal length ordering with the NMDS solution yielded a correlation of 0.9 ($p < 0.000001$). Parietal and temporal areas were maximally segregated, being joined at the one side by striate and prestriate areas, and at the other by STP and area 46. Hence, this method further corroborates the NMDS result. Simmen *et al.* do not explain how the excellent correspondence between four independent methods could come about by blind artefact.

The NMDS structures reported for all central sensory systems are curved. This does indeed reflect a principle of brain organization, though not a deep one: central sensory systems are all sparsely connected[12,15]. It is well-known that NMDS analysis of sparse similarity matrices produces curved structures[19]. NMDS faithfully reflects this *bona fide* aspect of data structure as it does more interesting ones.

We conclude that: (1) analysis of test data shows that solutions with fit in the range of the reported one can recover the structure of known input data almost perfectly; (2) the solution is not a low-fit one in which circular structure is likely to emerge artefactually; (3) independent analyses externally validate the result; (4) this validation extends to higher-dimensional solutions that would not have a planar circular form due to artefact. NMDS remains a potent means of analysing central nervous connectivity, which has already helped to identify the site of novel physiological features[20].

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Regional variation in fruitflies

SIR — Begun and Aquadro[1] estimate DNA variation, using four-cutter enzyme restriction analysis of genomic DNA, in two populations of *Drosophila melanogaster* from North Carolina and Texas, and one from Zimbabwe, and have compared their results on genetic structure with our published results. They conclude: (1) that the African population is more variable at the DNA level than those from the United States; (2) that most DNA restriction variants are not shared between the two geographical regions; and (3) that there is an unappreciated degree of population structure in *D. melanogaster* and the equilibrium models of molecular evolution are inappropriate for this species.

We wish to point out that although the African population studied in ref. 1 comes from a different region (East Africa) than those studied in our laboratory (West and Central Africa), we have reached similar conclusions using four-cutter restriction analysis of mitochondrial DNA variation[2–4]. The mtDNA variation data from a worldwide collection of lines show: (1) that intra-population diversity is about twice as high as that for the protein variation; (2) that population differentiation, as measured by the fixation index (F_{ST}), is roughly five times higher than that for a protein variation; and (3) that geographical populations of *D. melanogaster* harbour population and/or region-specific mtDNA haplotype(s).

Higher intra-population diversity for genomic DNA is expected (if for no other reason than the redundancy of the genetic code) and it is also expected that different genetic elements (for example, chromosome inversions, allozymes, DNA haplotypes and nucleotide sequence variation) with increasing power of resolution will show progressively higher levels of geographical differentiation. This is true of all species.

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BEGUN AND AQUADRO REPLY — A key difference between our study of nuclear genes and that of Hale and Singh on mtDNA is that the genetic history and potential of these *Drosophila* populations (in the broadest sense) is to be found in their nuclear DNA (the information content of mtDNA is minimal).

The qualitative trends of more variation in Africa and geographical differentation between Africa and US populations were seen both in Hale and Singh's data and in ours. However, our data are from a very large number of genetically independent nuclear gene polymorphisms, whereas the mtDNA data are from a single, non-recombining, maternally inherited marker. Therefore, one should have far more confidence in drawing general conclusions from our data.

Hale and Singh's points about the comparison of mtDNA and protein electrophoretic data are not relevant to our conclusion that the heterozygosity in Zimbabwe is greater than in the United States, based on comparison of an equivalent set of nuclear DNA markers. Although mtDNA may show greater geographical differentation than nuclear genes (as a result of the smaller effective size), there is no reason to expect that protein variation and nuclear restriction site polymorphism should show different degrees of population differentation (assuming that the observed variation has no fitness consequences). It is highly unlikely that the contrast between the level of protein polymorphism in West Africa and the level of DNA heterozygosity in Zimbabwe is simply explained by the higher resolution of restriction site analysis.

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