More on DNA typing dispute

SIR — Lander and Budowle[1] imply that the inferential problems of forensic genetics have been solved and that further studies are not warranted. Perhaps a spectator, with an interest in the more difficult, but equally confused, problems of linkage analysis could comment. The arguments of the authors and their associates instructed and entertained readers of *Science* two years ago in a series of articles when the differences in the misunderstandings of the various contestants were to some extent clarified. They have recently been catalogued and dissected in detail by Morton[2]. Different misunderstandings are hardly an adequate justification for gratuitous advice.

Forensic genetics covers a wide field, sometimes involving degraded specimens, or inferences on genetic mixtures on good samples (paternity tests), or the resolution of mixtures in degraded mixtures (rape). If there is an adequate supply of fresh blood, the various shot-gun methods pioneered by Jeffreys provide an unambiguous answer, but, as with ordinary fingerprints, convey too much information for mathematical analysis and are simple enough for judges and jurors to comprehend and interpret without advice. The quantity and quality of the blood available in the O. J. Simpson case was not stated.

If samples are limited or degraded, techniques involving amplification of short segments of DNA are necessary, and their analysis involves the summation of the evidence from each part. While it is obvious if any result differs, difficulties arise when they do not. This is the central problem of classification, and indeed of language, and can hardly be dismissed as a non-problem in a few pages.

Even the simplest model presents formidable difficulties. Suppose we have a bag of coins, one of which is double-headed. A coin is removed and tossed, and a decision with consequences of life or death has to be made on the result of a defined number of tosses of a single coin selected at random. If any tail appears, the problem is solved. If not, the odds against the coin selected being a regular coin after ten tosses are about a thousand to one. However, if there are a thousand coins in the bag, the odds against this coin having been selected are also a thousand to 1. It is not possible to give judgement without knowing the size of the bag, as Laplace observed in a similar context. In this case the regular coins are unbiased. In the forensic case of murder they are not. Murders preferentially involve relatives and neighbours.

Lander and Budowle's argument appears to be that if the bag were big enough to carry, and the coins of a regular variety, then we could assume a maximum size, or ceiling, and just keep tossing for as long as necessary. This is obviously true, but the 'ceiling' is so arbitrary that it can hardly 'support' any very elaborate inference. Even this has problems, for the 'regular' coins are not unbiased, as the population of the world does not consist of unrelated individuals: we are all relatives and most of us have several close relatives.

This introduces even graver problems if segments of chromosomes, as well as murderers, are assumed selected at random. A solution that could imply, at odds ratios comparable to the population of the world, that no two persons would have any realistic chance of being identical seems seriously flawed.

The courts will have enough problems in the O. J. Simpson case. It would be unfortunate if public appreciation of population genetics, a subject largely developed in the first half of this century, were to become one of comic denigration and add support for creationism and genetical brands of political correctness.

J. H. Edwards
University of Cambridge,
Genetics Laboratory,
Department of Biochemistry,
South Parks Road,
Oxford OX1 3QU, UK

SIR — Although the National Institute of Justice (NIJ) does not, as a general rule, take positions on issues of this sort, we wish to clarify one misunderstanding in the article by Lander and Budowle[1]. They write that: "The NRC [National Research Council] — at the urging of the National Institute of Justice, representing the academic wing of forensic scientists — has concluded that the best solution is to constitute another *ad hoc* committee on DNA fingerprinting, composed primarily of statisticians and population geneticists".

First, it is not the National Institute of Justice that urged the NRC to convene this board; the NRC jealously guards its independence. Several people suggested that a new committee be convened, including the director of the Federal Bureau of Investigation (FBI), William Sessions, in a letter to the NRC. NIJ was not one of those, but when the NRC decided to convene this committee, it approached NIJ for funding. At the urging of the FBI, and others, NIJ agreed to provide much of the funding for the new committee.

Second, the NIJ does not represent "the academic wing of forensic scientists". It doesn't represent any group of forensic scientists, academic or otherwise. It supports well-designed research into the forensic sciences by practitioners in crime laboratories, academics in universities and others, including work in the laboratories of federal law-enforcement agencies. Every peer-review panel at NIJ includes practitioners who ensure that NIJ research meets the real needs of US crime laboratories at the local, state and federal levels, as well as uniquely qualified experts from academic life and the federal and military forensic laboratories.

The role of the National Institute of Justice is unique. It serves as an independent research agency supporting all levels of the law enforcement and criminal justice system, from the local to the federal. It has, for nearly a quarter of a century, been the principal source of federal funds for the forensic sciences community and takes very seriously the legislative directive that it serve the practical needs of the law enforcement and criminal justice communities.

David G. Boyd
(Director, Science and Technology)
National Institute of Justice,
Washington, DC 20531, USA

SIR — Having been involved in several trials using DNA typing, I wish to reply to Lewontin and Hartl[3,4]. Lewontin states ". . .juries are no more capable of understanding probability statements than they are of interpreting any other piece of highly technical information. . ."[3].

Juries have been coping with probability statements with respect to serological typing with judiciousness and effectiveness for decades. DNA testing is not qualitatively different from serology. Perhaps Lewontin is reacting to the phenomenon that, with rare exceptions, judges and juries who have listened to his railing against DNA testing have chosen to be persuaded by the opposition's point of view. This does not prove that juries are incapable of understanding the issues, but merely attests to the lack of persuasiveness of Lewontin's arguments[3].

It is impossible to determine with certainty the genetic group or subgroup of any accused individual. Even in the rare instances when extensive pedigree information is available, experience with paternity testing has demonstrated that a significant fraction of paternity is misassigned. The use of the ceiling principle ensures that the suspect will be afforded the maximum conservatism with respect to the probability estimates and should not be considered an 'interim' solution.

I agree with Lewontin that the refusal by the FBI laboratory of outside inspection and data verification is troubling, especially when I have been called upon to testify in support of its findings. Regardless of the reasons for this policy, I believe that the FBI laboratory should be held to the same standards and requirements as other laboratories.

The term DNA fingerprinting, as I understand it, refers to a patented process of Cellmark Diagnostics involving multi-

locus probe testing. Therefore, as Lewontin points out, this term is used incorrectly throughout the Lander–Budowle article.

The continued existence of a Flat Earth Society and the increasing popularity of Creationism demonstrate that it is never possible to convince every individual of the validity of a scientific theory. However it is clear that the concepts of evolution and the spherical shape of our planet are "generally accepted" in the scientific community and would pass the Frye test for courtroom admissibility. *Nature*'s chronicle of the arguments against HIV as the causative agent of AIDS is another example of how a tiny, vocal minority with access to media outlets can attempt to sway public opinion against generally accepted medical and scientific opinions.

Charles M. Strom
Section of Medical Genetics,
Illinois Masonic Medical Center,
836 Wellington Avenue,
Chicago, Illinois 60657, USA

SIR — Lander and Budowle[1] highlight legitimate domains of convergence between two former opponents but stint on views of others and on unresolved issues. Lander and Budowle strongly doubt that the new NRC committee can make recommendations substantially to improve forensic DNA analysis. Recent correspondence by Lewontin[3] and Hartl[4] is largely tangential to that issue. Their letters consist mainly of speculation on the motives of individuals and the possible future behaviour of the FBI. Helpful comments by Lewontin on possible improvements in quality control and blind testing are diluted by other comments, for example his patronizing assertion that jurors are incapable of understanding the meaning of a 1 in 4 probability and his insistence that the situation is basically hopeless until an entirely different system for DNA identification is developed. New technologies for DNA identification are being developed and each will probably share some of the same problems in the current technology. Therefore, we need not wait for the millennium to find practical improvements. "A steady succession of *ad hoc* committees"[1] is undesirable, but significant work remains for the new NRC committee in advancing the way the existing technology is applied.

(1) Exceedingly small genotype frequencies (for example $<10^{-6}$) may be calculated and, to make the number smaller, one simply has to type more polymorphic loci. Such probabilities are presented to jurors who assess their meaning as best they can and with the assistance of experts such as Lewontin, Hartl and ourselves. However, it is fruitless, beyond a certain point, to continue to type additional markers when we are already as certain as we can be, based on *one* valid test, of genotypic identity. Lander and Budowle cite a frequency reported in one case, 1 in 738×10^{12}, as unrealistic, but provide no mechanism whereby the introduction of such a probability in a courtroom setting would be prevented or made sense of. Due to the possibility of error, exceedingly small genotype frequencies (say 10^{-7}) tell us little more than rare genotype frequencies (10^{-5}), but they may have prejudicial impact. It is more accurate to estimate a meaningful level of significance ($P<10^{-4}$ or $P<10^{-5}$).

(2) The first NRC committee suggested that genotype frequencies should be introduced with an error rate. Most practitioners of the forensic DNA art readily admit the possibility of error. Unfortunately, error rates are usually unavailable. Our suggestion in (1) would also mitigate this problem.

(3) Intrinsic to DNA testing are unique possibilities for eliminating error or fraud. We have two suggestions: (a) Different internal standards should be added to each sample to reveal sample mixing or mixups. (b) The individual performing an analysis should be unaware of which sample, out of a small group, derived from the suspect. This conforms to the established principle of blind testing.

(4) When, as frequently happens, multiple suspects are tested, the estimated match probability must be adjusted to take into account multiple testing. The NRC committee should also develop guidelines for the use of large databases of DNAs from criminal suspects.

(5) Special circumstances warrant the abandonment of the genotype frequency as the match probability. If individuals with a high degree of kinship have not been ruled out as the perpetrator, then the probability of the match is not the genotype frequency (and *pari passu*, idiotyping by DNA sequencing, as suggested by Lewontin, might exacerbate this problem). People differ in the number of close relatives they have; some have many close relatives, and inbreeding can enhance genetic identity by descent. Many individuals have half- or full-siblings unknown to them. As frequencies become increasingly remote, remote considerations loom increasingly large.

(6) What is the relevant genotype frequency, that of the evidence or that of the suspect?

(7) The ceiling principle method was formulated to account for possible differences in allele frequencies between populations. The second NRC committee should emphasize that the same considerations universally apply, for example to DQα.

The first NRC committee provided sound and conservative methods. Although conservative, the ceiling principle is arbitrary. Therefore it is doubtful if it would ever have been implemented save with the imprimatur of a distinguished committee. So far only the modified ceiling principle has been used because the systematic sampling of populations suggested by the NRC has not been performed. The second NRC committee is now in a unique position to refine the use of forensic DNA testing in important ways and to reexplore useful suggestions made by the first NRC committee but only partially implemented.

David Goldman
Jeffrey Long
National Institute on Alcohol Abuse and Alcoholism,
Intramural Research Program,
Rockville, Maryland 20852, USA

1. Lander, E. S. & Budowle, B. *Nature* **317**, 735–738 (1994).
2. Morton, N.E. *Eur. J. Med. Gen.* **1**, 172–178 (1993).
3. Lewontin, R. C. *Nature* **372**, 398 (1994).
4. Hartl, D. L. *Nature* **372**, 398–399 (1994).
5. East, E. M. *Bot. Gaz.* **57**, 239 (1914).
6. Nägeli, K. W. Mechanisch-Physiol. Theorie der Abstammungslehre (München, Oldenburg, 1984).
7. Baird, H.W. *Lancet* **II**, 1250 (1968).
8. Slatis, H.M. *et al. Am. J. hum. Genet.* **28**, 280 (1976).

SIR — Lewontin and Hartl[3,4] complain that "because juries are no more capable of interpreting probability statements than they are of interpreting any other piece of highly technical information, there are insuperable barriers to their use in the courts". Perhaps I should recall the words of E. M. East, the pioneer quantitative geneticist[5] commenting on Edgar Allan Poe: "as a poet and mathematician, he would reason well, as a mere mathematician he would not have reasoned at all." I am not surprised that lay people may be confused when some the terms used by Lewontin are also ill defined. The word 'idioplasm' was coined by Karl Wilhelm Nägeli[6] before the Mendelian concepts became known and he used it in the sense of the entirety of the hereditary material. The newly developing genetics, after the turn of the century, abandoned this term for the more meaningful gene and genotype. Immunogeneticists revived it in the form of idiotope, the antigenic determinants in the variable chains of the immunoglobulins and idiotype as a collection of idiotopes distinguishing one type of antibody-producing cells from other clones of cells. Thus it is not a concept of DNA but of a protein and this is worth remembering even now, 30 years after synonymous codons became known. Thus, obviously it is not correct to call fingerprints — and I do not mean DNA fingerprints — idiotype(s). Also, it is well documented that some kindreds display no dermatoglyphs[7]. In some instances, forensic genetics cannot rely with absolute certainty on dermatoglyphics because of developmental differences, mosaicism and more than single gene involvement in the pattern[8].

G. P. Rédei
3005 Woodbine Court,
Columbia, Missouri 65203, USA