Author's Response

Sir:

In a recent JFS paper (1), we modeled the multi-locus DNA mixture problem using coupled linear equations. Our general matrix equation combines genotypes with mixture weights, thereby predicting relative peak intensity. Matrix methods can help solve this equation. We called our approach "linear mixture analysis," or "LMA."

We showed how LMA can model a typical rape case—a two-person multi-locus mixture containing a known reference and an unknown contributor. To automatically solve this class of problems by computer, we devised a least squares minimization method (which we dubbed "mixture deconvolution") that simultaneously estimates the genotype of the unknown contributor, along with the mixture weights. The method of least squares was developed by Gauss and others in the 19th century. It can be used to solve linear equations, and has been applied to the one locus DNA mixture problem (2).

While Dr. Wang expresses concern about whether our presentation will be understood by the general reader, we see no merit to her concerns. Specifically:

- The equation involving matrix division was chosen by the publisher for clarity. Instead of "w = G\d", they used the formal division notation "_". There was no loss in meaning, especially because the sentence explicitly states that this MATLAB matrix division was done "using the built-in matrix [left] division operation "\"."
- MATLAB automatically handles the case of partial rank by using a statistically robust generalized matrix inverse. MATLAB's approach is a key advantage of using a validated high-level numerical programming language. Moreover, with the powerful multi-locus methods described in our manuscript, the hypothetical partial rank situation does not occur in real mixture problems.
- The matrix notation was chosen by the publisher. Because the text explicitly states when a matrix is being used (e.g., "matrix equation") and when a scalar is being used (e.g., "w in (0,1)"), no reader will be confused.
- Regarding three person mixtures, the paper describes how a mixture deconvolution algorithm was used to determine an unknown genotype. Also mentioned in the paper was our use of the LMA model to solve mixture problems in the absence of reference profiles. We are currently validating these more general LMA methods.

Point estimates (e.g., those determined by least squares methods) can completely solve a problem when there is a unique solution. Real data often have greater uncertainty, and these estimates then form a useful starting point for further computation. Our forensic goal is to objectively and automatically determine the reasonable set of suspect genotypes that are compatible with the DNA evidence. Our approach to achieve that goal will be described in future publications.

References

1. Perlin MW, Szabady B. Linear mixture analysis: a mathematical approach to resolving mixed DNA samples. J Forensic Sci 2001;46(6):1372–7.
2. Gill P, Sparkes R, Pinchin R, Clayton TM, Whitaker JP, Buckleton J. Interpreting simple STR mixtures using allele peak area. Forensic Sci Int 1998;91:41–53.

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