A41 Error Tradeoffs in Human Identity Comparisons: Determining a Complexity Threshold and Exclusion Criteria for DNA Mixture Interpretation

Jacob S. Gordon, MS, Boston Univ, Biomedical Forensic Sciences, 72 E Concord St, Rm R806D, Boston, MA 02118; Robin W. Cotton, PhD, Boston Univ, Biomedical Forensic Sciences, 72 E Concord St, L1004, Boston, MA 02118; and Catherine M. Grgicak, PhD, Boston Univ, Biomedical Forensic Sciences, 72 E Concord St, Rm R806D, Boston, MA 02118*

This goal of this presentation is to introduce an alternative framework for making determinations of exclusion versus inclusion for DNA mixtures that is based on running Monte Carlo simulations on a probabilistic computer model of individual and mixed human genotpyes. This method is then applied to laboratory mixture data, and the results are compared with those for the simulated mixtures.

This presentation will impact the forensic science community by emphasizing how error rates associated with DNA profile interpretation are crucial to responsible determinations of a reference's exclusion or inclusion in an evidence sample. The error characterizations demonstrated in this study are useful in a number of ways. The simulated results can be used by a laboratory to inform the establishment of a preferred interpretation range by selectively optimizing between false positives and false negatives. Alternatively, after empirically determining a level of drop-out associated with evidence samples of varying starting DNA template, an informed decision regarding exclusion of a known as a potential contributor to an item of evidence will be presented. Traditionally, such samples were reported as uninterpretable or inappropriate for comparison.

DNA analysts considering a forensic evidence sample and a reference sample (e.g., from a suspect) have three options when rendering a decision with regard to the consistency between the samples: exclusion, inclusion, and inconclusive. Complicating this determination is the reality that DNA profiles originating from forensic mixture evidence may not be fully observed due to allelic drop-out and/or the presence of overlapping alleles. Different analyst inclinations and laboratory standards exist for informing an analyst's decision; typically—and particularly for samples demonstrating some degree of allelic drop-out—less than exactly 100% allelic consistency between known and questioned samples are not automatically precluded from inclusion in an evidence sample. In tolerating some measure of absence of a reference sample's alleles in an evidence sample, the potential for two kinds of errors exists: In a case in which an individual could not have contributed to an evidence sample, there is the potential for false inclusion; in a case in which an individual could have contributed, there is the potential for false exclusion. In selecting a particular decision criterion to inform determinations of inclusion or exclusion, a tradeoff between these errors exists. A lax decision criterion minimizes false exclusions at the expense of false inclusions while a strict criterion eschews false inclusions at the expense of greater numbers of false exclusions. The relevance of a decision criterion is greatest for low-template samples and for samples that are mixtures of multiple contributors since both are likely to experience allelic drop-out and thus to occupy a potential gray area between certain exclusion and likely inclusion.

In this study, for a given level of allelic drop-out, 10,000 simulated mixtures are compared with databases of 10,000 simulated excluded and included reference individuals. In order to generate credible genetic profiles, the phenomena of allelic drop-out and profile mixing of two contributors are modeled. Comparisons between the reference and simulated mixtures at drop-out levels ranging from 0 to 0.9 are performed. Given this framework, the universe of possible decision criteria is explored. Receiver Operating Characteristic (ROC) curves, a type of analysis originally applied to assessing World War II radar performance, are adopted as a paradigm for summarizing the tradeoff of both types of errors and confirm that higher rates of drop-out result in increasingly higher incidences of error. Specifically, ROC analysis of the two-person mixtures showed that drop-out rates >0.3 result in false positive rates >0.01 and false negative rates >0.15. Here the false positive rate represents the proportion of reference standards that were incorrectly included as a potential contributor. The false negative rate is the proportion of standards that were incorrectly excluded.

ROC analysis can be used to inform the establishment of a preferred operating point by selectively optimizing between false positives and false negatives to accord with prudence. Alternatively, after empirically determining a level of drop-out associated with a particular laboratory or with evidence samples of varying starting DNA template, an informed decision can be made regarding the number of allelic discrepancies that may be tolerated before that rate of false inclusions becomes too large.

The specification of error bounds can also designate an operating region, outside of which the interpretation of an evidence profile cannot be made with the required accuracy. Whether a given evidence profile is a candidate for interpretation is a function of its associated level of drop-out. Evidence profiles shown to lie outside of the acceptable error bounds due to their level of allelic drop-out are said to fail to meet a "complexity threshold" for determinations of inclusion or exclusion. No statistics should be calculated for such samples, and the only responsible determination with respect to reference inclusion/exclusion is "inconclusive" or "uninterpretable." For evidence profiles possessing levels of drop-out that are deemed interpretable, this same "complexity threshold" can be employed to establish a laboratory's decision criteria with respect to tolerating allelic discrepancies. The resulting prescription for determining that a reference is included as a contributor to an evidentiary stain would conform with premeditated, laboratory-

 ** Presenting Author*

selected error rates and the decision regarding whether to compare the questioned sample to a reference would be made before examining a known DNA profile.

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 ** Presenting Author*