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An assessment of the information content of likelihood ratios derived from complex mixtures

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ABSTRACT

With the increasing sensitivity of DNA typing methodologies, as well as increasing awareness by law enforcement of the perceived capabilities of DNA typing, complex mixtures consisting of DNA from two or more contributors are increasingly being encountered. However, insufficient research has been conducted to characterize the ability to distinguish a true contributor (TC) from a known non-contributor (KNC) in these complex samples, and under what specific conditions. In order to investigate this question, sets of six 15-locus Caucasian genotype profiles were simulated and used to create mixtures containing 2–5 contributors. Likelihood ratios were computed for various situations, including varying numbers of contributors and unknowns in the evidence profile, as well as comparisons of the evidence profile to TCs and KNCs. This work was intended to illustrate the best-case scenario, in which all alleles from the TC were detected in the simulated evidence samples. Therefore the possibility of drop-out was not modeled in this study. The computer program DNAMIX was then used to compute LRs comparing the evidence profile to TCs and KNCs. This resulted in 140,000 LRs for each of the two scenarios. These complex mixture simulations show that, even when all alleles are detected (i.e. no drop-out), TCs can generate LRs less than 1 across a 15-locus profile. However, this outcome was rare, 7 of 140,000 replicates (0.005%), and associated only with mixtures comprising 5 contributors in which the numerator hypothesis includes one or more unknown contributors. For KNCs, LRs were found to be greater than 1 in a small number of replicates (75 of 140,000 replicates, or 0.05%). These replicates were limited to 4 and 5 person mixtures with 1 or more unknowns in the numerator. Only 5 of these 75 replicates (0.004%) yielded an LR greater than 1,000. Thus, overall, these results imply that the weight of evidence that can be derived from complex mixtures containing up to 5 contributors, under a scenario in which no drop-out is required to explain any of the contributors, is remarkably high. This is a useful benchmark result on top of which to layer the effects of additional factors, such as drop-out, peak height, and other variables.

1. Introduction

As a consequence of both the increasing sensitivity of DNA typing methodologies, as well as mounting awareness by law enforcement of the perceived capabilities of DNA typing, complex mixtures consisting of DNA from two or more contributors are increasingly being encountered in forensic DNA profiles (N. Rudin and K. Inman, personal communication; [1–6]).

At least two factors may reduce the information content of multi-contributor samples as compared with single source samples. First, many of the possible alleles at a particular locus may be present in the evidence sample, diminishing the ability to exclude people as contributors to the mixture. Second, two or more contributors to the mixture may share the same alleles, increasing the difficulty of inferring the genotypes of the true contributors (TCs) of the mixture directly from the evidentiary sample. Together, these factors reduce the ability to distinguish TCs from known non-contributors (KNCs) in complex mixtures. These difficulties are exacerbated by forensic DNA evidence samples compromised by various conditions, such as low quantity and poor quality, that result in complex profiles exhibiting characteristics

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such as allelic drop-out, degradation, inhibition, peaks heights that do not reliably reflect the original contribution to the sample, and varying ratios of multiple contributors. In this work we focus on separating out the effects of multiple contributors.

Historically, binary approaches, such as combined probability of inclusion (CPI), and restricted or modified random match probability (RMP) have been used to estimate the evidential strength of mixed samples in forensic DNA analysis [7–10]. More recently, the likelihood ratio (LR) approach is gaining acceptance as a tool to estimate the weight of complex profiles [2,3,5]. The LR represents the ratio of probabilities of observing the alleles detected in an evidence profile under two mutually exclusive hypotheses, represented as the numerator (H_1) and denominator hypotheses (H_2). LR values greater than 1 are interpreted as indicating greater support for H_1 than H_2, whereas a LR less than 1 indicates greater support for H_2 than H_1 [11,12]. The standard mathematical depiction of the LR is:

$$\mathrm{LR} = \frac{\Pr(E|\mathrm{H}_1)}{\Pr(E|\mathrm{H}_2)}$$

Calculation of a LR requires specification of the total number of contributors, as well as the number of contributors meeting various conditions for both H_1 and H_2.

For situations encountered in forensic DNA, three categories of conditioned contributors are frequently encountered. The first category is an individual whose DNA is assumed present, usually because of the nature of the sample; this conditioned contributor is often categorized as "assumed." Contributors in this category are assumed to be present and therefore are conditioned contributors in both the numerator (H_1) and denominator (H_2). The second category is an individual for whom the weight of evidence is being assessed; this conditioned contributor is often characterized as a "suspected" or "hypothesized" contributor [13]. Contributors in this category follow different conditions in H_1 and H_2; typically this contributor is conditioned in H_1 and replaced with an unknown contributor in H_2. The third category is a contributor whose profile is unknown (unprofiled); unknown individuals are invoked to complete the total number of contributors.

Taking the simplest example, a single source sample, the numerator hypothesis would typically pose that the evidence derives from a single known individual (i.e. a profiled hypothesized contributor), whereas the denominator hypothesis replaces this known individual with an unknown (i.e. unprofiled) individual. In contrast, the hypotheses for mixtures expand to consider varying numbers of assumed, hypothesized and unknown contributors; thus, multiple pairs of competing hypotheses might be considered for a particular mixed sample. For example, under the assumption of a two person mixture, H_1 could posit that the evidence sample derives from one hypothesized and one assumed contributor, while the H_2 hypothesis might be that the evidence is explained by one unknown plus one assumed contributor. An alternative pair of hypotheses for the same mixture could be that under H_1 the mixture derives from one hypothesized contributor and one unknown contributor, while under H_2 the mixture derives from two unknown individuals.

Intuitively, we expect that a TC included in the numerator hypothesis should result in a $LR > 1$, indicating support for the proposition that the TC actually contributed to the sample. Conversely, we expect that a KNC assumed in the numerator hypothesis should result in a $LR < 1$, indicating support for the proposition that an unknown contributor is the TC to the sample. However, it has been shown that under certain scenarios these simplistic expectations fail. The earliest mention of this possibility surfaced when Evett [14] demonstrated that a two person mixture could yield a $LR < 1$ even when there existed confirmatory information for H_1, the numerator proposition (which Evett described as the 'prosecution proposition'). Much later, Brenner et al. [15] commented that altering the proposed number of contributors will change the LR from $LR > 1$ to $LR < 1$ when the hypothesized contributor carries the more common alleles in the mixture. Shortly thereafter, Weir et al. [8]. using the historical Polymarker® genetic typing kit on mixtures, showed that TCs may generate $LRs < 1$. Specifically, if all of the alleles at a particular locus were detected in the evidence profile, and the hypothesis in the numerator included at least one unknown contributor, the resulting LR could be less than 1 if the hypothesized contributor in the numerator carried common alleles at the locus. A small body of work suggests that, especially for mixtures, some non-trivial proportion of KNCs will generate $LRs > 1$ [16–19]. This is not only unsurprising, but statistically predicted. For example, when Gill et al. [16] proposed a method for measuring the robustness of an LR, they illustrated that simulated KNC profiles could produce $LRs > 1$. However, they only tested its usefulness on a handful of casework stains.

In spite of this earlier work, we are not aware of any published research that assesses how often these effects would be expected to occur in different types of mixtures, or to explore how different genotypes for the hypothesized contributor, might affect the results. In particular, the moderately variable loci typed in current short tandem repeat (STR)-based systems potentially give rise to the situations in which the LR for a TC included in the numerator hypothesis falls below 1, as well as those in which a KNC produces a $LR > 1$. Determining the frequency with which these effects occur, and under which particular circumstances, would add greatly to our understanding of the LRs produced for complex profiles.

As advances in technology began to allow laboratories to analyze challenging samples, it became immediately and abundantly clear that the community did not have the appropriate tools, nor the supporting research, to reliably interpret and weight the resulting complex profiles. Over the past few years, research on using LRs to assist in interpreting these profiles has produced publications on a number of issues, including the ability to estimate the number of contributors [20–25] and the effect of mis-specifying the number of contributors when computing LRs [24]. While Gill, et al. [16] proposed a method (implemented in LRMix [26]) to calculate the probability of a misleading LR, they incorporated the probability of both dropout and drop-in, but did not isolate the parameters of allele frequencies or number of contributors. We are not aware of any studies that systematically address how varying only the number of contributors and unknown contributors affects the ability to distinguish TCs from KNCs in mixed samples. Published studies [17,27,28] attempt either to separate the effects of multiple contributors from other variables, such as low template, drop-out, drop-in or peak heights, or focus on simpler hypotheses involving fewer contributors.

Unlike the LR, the CPI (aka random man not excluded, RMNE) does not require specification of the number of contributors in the sample. The lack of requirement to specify the number of contributors, combined with the ease of calculation, and perceived simplicity of explanation, has resulted in the widespread use and acceptance of this calculation. However, the CPI has been strongly criticized in the literature (reviewed in [1,7,29,30]) both because it discards information, and also because, in certain situations, it can be prejudicial to the hypothesized contributor for a variety of reasons [1,2,4,29–32].

Here, we aim to explore the capabilities and limitations of statistical approaches used to assess the strength of evidence derived from complex DNA mixtures based solely on the number of contributors (ranging from 2 to 5) and the frequency of alleles found in commonly-used STR loci. Nominally, we assessed how often and under what conditions TC generate $LRs < 1$ (termed