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Match likelihood ratio for uncertain genotypes†

MARK W. PERLIN*
Cybergenetics, Pittsburgh, PA 15213, USA

JOSEPH B. KADANE
Statistics Department, Carnegie Mellon University, Pittsburgh, PA 15213, USA

AND

ROBIN W. COTTON
Biomedical Forensic Sciences, Boston University School of Medicine, Boston, MA 02118, USA

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Genetic data are not necessarily fully informative, leading to uncertainty in an inferred genotype. The posterior genotype probability distribution incorporates the identification information present in the data. To compare uncertain genotypes, we introduce here a match likelihood ratio (MLR), a simple generalization of the likelihood ratio standardly used to understand the import of genetic evidence in forensic applications. The MLR gives the relative probability of a match between questioned evidence and a suspect, with respect to a match between the evidence and a relevant population. Coancestry can be naturally incorporated. We present illustrative examples and provide a detailed analysis and comparison for a two-person DNA mixture. We describe MLR's computation efficiencies when making multiple genotype comparisons and show how MLR was used to explain evidence in court. As statistical computing of forensic DNA inferences becomes more commonplace, the MLR may help in quantifying match identification information.

Keywords: coancestry; DNA; evidence; genotype; likelihood ratio; match; probability.

1. Introduction

DNA is a powerful identification methodology that helps solve crimes (Butler,2005). Biological specimens are collected as crime scene evidence. Scientists generate short tandem repeat (STR) laboratory data (Edwards *et al.*, 1991) from these specimens and then infer DNA genotypes from the observed STR data peaks. By comparing these evidence genotypes against the genotypes of possible suspects (including DNA databases), matches between genotypes can help identify individuals who contributed their DNA to the evidence.

The observed genetic data do not always specify a genotype with certainty. Computer systems have been developed that infer uncertain genotypes from kinship (Hilden, 1970; Heuch and Li, 1972)

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* Email: perlin@cybgen.com

and DNA mixture (Mortera *et al.*, 2003; Perlin, 2003; Bill *et al.*, 2005; Wang *et al.*, 2006) data. These systems may produce multiple genotype values at a locus and assign probabilities or likelihoods to the possible values.

When comparing an uncertain DNA mixture genotype with a reference, many approaches use only the most likely genotype values. Some just select a single genotype value having a maximum likelihood for reference comparison (Perlin and Szabady, 2001; Wang *et al.*, 2006; Cowell *et al.*, 2007). Other approaches select a subset of highly likely genotype values (SWGDAM, 2000; Bill *et al.*, 2005; Curran, 2008). An alternative DNA mixture approach is to use a likelihood ratio (LR) of a joint likelihood for the mixture data relative to the marginal likelihoods (Evett *et al.*, 1998), integrating over all feasible genotype values. A LR method (Good, 1950; Roeder, 1994) is attractive because it uses effectively the match information present in the data (Gill *et al.*, 2006).

Some computer systems use Bayesian inference to obtain a posterior genotype probability mass function (pmf) that summarizes the data identification information (Perlin, 2003; Curran, 2008). The posterior genotype pmf generally contains more information than a single maximum likelihood genotype value or a subset of highly likely values (O'Hagan and Forster, 2004). A LR formulation based on the posterior genotype would not need to revisit the original data. This paper introduces a *match likelihood ratio* (MLR) that directly compares uncertain genotypes to provide a match rarity statistic.

We begin by describing the uncertain genotypes that will be used in the MLR. We then show how genotype match can be represented as a probability of genotype equality, and how to compute that probability, touching briefly on coancestry considerations. We next define the MLR as a ratio of two genotype match probabilities and show that the MLR is indeed a LR. We briefly describe some illustrative examples to show how MLR works. We then analyse one DNA mixture example in some detail, computing a MLR for a published posterior distribution genotype and comparing that result with a less informative genotype. We consider how MLR accelerates LR computation with investigative DNA databases. We also report on how we used MLR to help explain DNA mixture evidence in court. We conclude with a discussion of how the MLR can be used in forensic practice.

2. Uncertain genotypes

A single source DNA reference sample usually yields an unambiguous genotype at each genetic locus. However, crime scene evidence is often more complex. Evidence can have low levels of DNA, damaged DNA or contain mixtures of DNA from multiple contributors. The result is that there may be considerable uncertainty in the genotypes inferred from the data. The genetic uncertainty at a locus can be described by associating a probability with each genotype value. The genotype's probability distribution characterizes the information learned from examining the DNA data using a particular interpretation method.

Starting from questioned sample data d_Q, a forensic scientist can apply a DNA interpretation method and infer a questioned genotype Q (Table 1). A population allele data set d_R can be used to infer a relevant population genotype R that gives relative frequencies of genotype occurrence based on population proportions. From a possible suspect's data d_S, a known suspect genotype S can be inferred. We assume that all of these data are independent of each other.

An individual's genotype at a genetic locus has some allele pair value. Let X be a fixed finite set of all such allele pair possibilities. When there is uncertainty in an inferred genotype, the genotypes

TABLE 1 *For each of three genotype classes (questioned evidence, relevant population and suspect profile), the notation for its associated data, genotype and pmf is shown*

	Data	Genotype	pmf
Questioned evidence	d_Q	Q	$q(x)$
Relevant population	d_R	R	$r(x)$
Suspect profile	d_S	S	$s(x)$

Q, R and S become random variables on set X. These genotypes have respective pmfs $q(x)$, $r(x)$ and $s(x)$, where x is a genotype value in X (Table 1).

Uncertain genotypes regularly appear in forensic DNA practice, although their description may be intertwined with some specific match statistic. For example, the probability of inclusion (PI) statistic[1] (SWGDAM, 2000; Budowle *et al.*, 2009c) can be viewed as a method of inferring genotype Q from DNA mixture data as a list of allele pairs and then matching its uniform genotype pmf with a unique suspect genotype S (see Section 5). Observed genotype frequencies represent a sample from a relevant population described in random variable R. The relevant population may be an ethnic subgroup (National Research Council, 1996) or one that does not contain the suspect (Balding, 2005). Genotype R may also describe a distribution for some other alternative hypothesis.

3. Genotype match

A match event between the two genotypes Q and S occurs when $Q = S$. We are interested in the probability of this match event, or $\Pr\{Q = S\}$. We observe that the probability of two genotypes sharing a common value is the sum of joint probability events over all the disjoint genotype values x in the value set X

$$\Pr\{Q = S\} = \sum_{x \in X} \Pr\{Q = x \ \& \ S = x\}.$$

Each joint probability term can be factored using conditional probability to form the sum of products

$$\Pr\{Q = S\} = \sum_{x \in X} \Pr\{Q = x | S = x\} \cdot \Pr\{S = x\}.$$

To avoid examiner bias (National Research Council, 2009), we assume that an objective analyst inferred the questioned genotype Q without any knowledge of the suspect's genotype S. Therefore, the probability of the questioned genotype at any value is independent of the suspect's genotype, or, $\Pr\{Q = x | S = x\} = \Pr\{Q = x\}$, and so

$$\Pr\{Q = S\} = \sum_{x \in X} \Pr\{Q = x\} \cdot \Pr\{S = x\}.$$

The analyst's genotype inferences for Q and S included their respective pmfs $q(x)$ and $s(x)$. Therefore, the match probability between the questioned genotype and the suspect is the sum of genotype

[1] This inclusion statistic goes by several names, including "combined probability of inclusion" (CPI) and "random man not excluded" (RMNE).

probability products

$$\Pr\{Q = S\} = \sum_{x \in X} q(x) \cdot s(x). \tag{1}$$

By similar reasoning with genotypes Q and R, we also conclude that the match probability between the questioned genotype and some relevant population is the sum of genotype probability products

$$\Pr\{Q = R\} = \sum_{x \in X} q(x) \cdot r(x). \tag{2}$$

DNA samples having identical genotypes may share a common ancestry (Balding and Nichols, 1994) and so are not necessarily independent. The *coancestry coefficient* θ is the probability that a randomly selected allele shared by two genotypes is identical by descent. We can write the theta-dependent genotype match probability between Q and S (and similarly for Q and R) as the sum of products

$$\sum_{x \in X} q(x) \cdot s(x) \cdot \mu_{QS}(\theta, x). \tag{3}$$

We define the *coancestry measure* $\mu_{QS}(\theta, x)$ as the ratio of the joint posterior genotype probability to the product of the marginal posterior genotype probabilities. We can calculate this measure by rearranging the posterior probabilities with Bayes theorem (Feller, 1968) and then substituting in the standard Dirichlet representation of population allele frequencies (Evett and Weir, 1998).

4. Match likelihood ratio

We define the MLR as the probability of a match between genotypes Q and S relative to the probability of a match between Q and R.

$$\text{MLR} = \frac{\Pr\{Q = S\}}{\Pr\{Q = R\}}. \tag{4}$$

This match rarity statistic can be reported by reading from formula (4) the statement:

> a match between the genotypes of the evidence and the suspect is (some number) times more probable than a match between those of the evidence and a random person,

or, more colloquially,

> a match between the evidence and the suspect is (some number) times more likely than a match between the evidence and a random person.

We need to show that the MLR is actually a LR. Bayes theorem tells us that the evidence information can be summarized in a LR (Lindley, 2006). The LR compares the probability of the evidence (E), conditioned on a hypothesis (H) and background knowledge (K) to the evidence probability conditioned on the negation of H ($\sim H$), along with K. The genotypes Q, R and S, along with their pmfs, provide the background information K. By ignoring the prior odds ratio, the LR focuses on how well the hypothesis explains the evidence (Aitken and Taroni, 2004).

The symbols E, H and K denote propositions, where 'a proposition is defined to be a statement where it is meaningful to assert that it is true or that it is false' (Good, 1950, p. 1). Forensic DNA

interpretation has customarily used the symbol E to denote an evidence proposition about some function of the observed STR data peaks (Evett and Weir, 1998), thereby forming a data likelihood ratio (DLR). However, a valid LR construction (Good, 1950, chapter 6) need not adhere to this particular DLR convention. Since our approach compares genotypes (whose inference has already summarized the STR data), it is more natural in this situation to have the evidence proposition E describe a (true or false) match event between two genotypes.

The evidence proposition E that we are concerned with here is an observed event $Q = U$ that there is a match between the inferred questioned genotype Q and a genotype U belonging to an unknown person. The standard prosecutor's hypothesis H is that the unknown person is the suspect; hence, genotype U is the genotype S. The alternative hypothesis $\sim H$ (e.g. propounded by the defense) is that the unknown is not the suspect, but instead some other person in a relevant population, and so genotype U is the population genotype R. Therefore, the standard LR based on this genotype match evidence compares the alternative hypotheses as follows:

$$\begin{aligned}\mathrm{LR} &= \frac{\Pr\{Q = U | H, K\}}{\Pr\{Q = U | \sim H, K\}} \\ &= \frac{\Pr\{Q = U | U \text{ is } S\}}{\Pr\{Q = U | U \text{ is } R\}}.\end{aligned}$$

After substituting in the appropriate conditioned genotypes, we obtain the MLR defined in (4)

$$= \frac{\Pr\{Q = S\}}{\Pr\{Q = R\}} = \mathrm{MLR},$$

which establishes that the MLR is the standard forensic identity LR.

Combining the MLR probability ratio of (4), together with the sum of product formulas (1) and (2), we obtain the MLR sum of products ratio evaluation form

$$\mathrm{MLR} = \frac{\sum_{x \in X} q(x) \cdot s(x)}{\sum_{x \in X} q(x) \cdot r(x)}. \tag{5}$$

Accounting for coancestry using (3) would give a theta-adjusted MLR as

$$\mathrm{MLR}(\theta) = \frac{\sum_{x \in X} q(x) \cdot s(x) \cdot \mu_{QS}(x, \theta)}{\sum_{x \in X} q(x) \cdot r(x) \cdot \mu_{QR}(x, \theta)}. \tag{6}$$

5. Illustrative examples

We illustrate the application of the MLR by using the sum of probability products ratio (5) to compute some useful DNA match statistics.

1. *Single source*. When the questioned evidence and the suspect both come from clean single source DNA, their respective independent genotypes Q and S each have a unique allele pair value. Therefore, pmfs $q(x)$ and $s(x)$ both have a probability of 1 at their respective genotype values and are equal to 0 at all other values. When Q and S agree on the same genotype value x_0, the MLR numerator is 1 and the denominator reduces to the population genotype frequency $r(x_0)$. The MLR statistic (5) thus reproduces the simple random match probability estimate $\frac{1}{r(x_0)}$. This overestimate can be corrected to account for coancestry (Balding and Nichols, 1994) using the theta-adjusted MLR of (6).

2. *Kinship*. Suppose that the questioned evidence has a unique genotype Q but that the suspect genotype S is inferred genetically from his or her mother and father. Then, S has a probability distribution $s(x)$, with possible Mendelian values of 1/4, 1/2 or 1 at each locus. (More informative, and commensurately more complex, S genotype pmfs would also incorporate the likelihood of offspring [Sisson, 2007], but these are not introduced here.) Unique genotype Q can be compared with this uncertain genotype S to find a match probability $\Pr\{Q = S\}$. The computed MLR from (5) normalizes this factor by a match probability $\Pr\{Q = R\}$ between Q and the relevant population genotype R to determine the match rarity. Accounting for coancestry using (6) sharpens this approximation to produce the exact LR.
3. *Mixtures*. Now suppose that suspect genotype S is unique but that questioned genotype Q is from a DNA mixture with n visible allele peaks. There are $N = \frac{n(n+1)}{2}$ unordered pairings of the n alleles. Thus, one might infer a list of these N possible genotype values x, assigning each one the same uniform probability $q(x) = \frac{1}{N}$, and all other values probability 0. Suppose that there is a matching suspect genotype S (having a known allele pair) at one of these genotype values. With allele frequencies $p_1, p_2, \ldots, p_n$, the genotype R has probability p_i^2 for homozygote values and $2p_i p_j$ for heterozygote values. By substituting the genotype pmfs $q(x)$, $r(x)$ and $s(x)$ into the MLR expression (5), we derive the standard PI match statistic (CPI and RMNE) that many workers use to interpret DNA mixtures (SWGDAM, 2000).

$$\mathrm{MLR} = \frac{\sum_{x\in X} q(x)\cdot s(x)}{\sum_{x\in X} q(x)\cdot r(x)} = \frac{\frac{1}{N}\cdot 1}{\frac{1}{N}\cdot(p_1^2 + 2p_1p_2 + \cdots + p_n^2)} = \frac{1}{(p_1 + p_2 + \cdots + p_n)^2}.$$

4. *Missing persons*. We can compare an evidence genotype Q (mixture example 3) with an inferred Mendelian reference genotype S (kinship example 2). Substituting their genotype pmfs, along with the pmf of relevant population genotype R, into the MLR equation (5) determines match rarity as a LR. This approach is useful in mass disasters, where damaged DNA remains produce an uncertain questioned genotype Q (Perlin, 2007) that can be compared with a missing person genotype S reconstructed from family genotypes (Heuch and Li, 1972).

   Note that for the single source (Example 1) and the inclusion probability distributions appearing in simple kinship and DNA mixture analysis (Examples 2 and 3), the MLR sum of products ratio reduces to a familiar reciprocal of a sum of population genotype probabilities. This symmetrical form may not occur with uncertain genotype comparisons (Example 4) that have unequal genotype probabilities. With such nonuniform genotype pmfs, the MLR is calculated using formula (5).

6. Mixture example

It would be instructive to see how MLR is used with a posterior genotype pmf for a two-person DNA mixture and then compare the genotype match information with that obtained using a maximization approach. In this mixture example, questioned major contributor genotype Q was inferred in a Markov chain Monte Carlo (MCMC) computation from a hierarchical Bayesian model (Curran, 2008, figure 3, blue bars) using quantitative STR peak height mixture data (Wang *et al.*, 2006, table 10). We constructed a relevant population genotype R using a standard Caucasian allele frequency database (Budowle *et al.*, 1999). The suspect genotype S was known (Wang *et al.*, 2006, table 10).

TABLE 2 (a) *The genotype probabilities and MLR calculation are shown for the posterior distribution genotype Q inferred by Curran at locus D13S317 that has unequal q(x) probabilities.* (b) *The MLR calculation is shown for a uniform genotype Q' inferred as a subset of D13S317 allele pair values that have equal $q'(x)$ probabilities*

(a)

		Genotype probability distributions			Match probabilities	
Allele pair		Q	R	S	$\Pr(Q = S)$	$\Pr(Q = R)$
x		$q(x)$	$r(x)$	$s(x)$	$q(x) \cdot s(x)$	$q(x) \cdot r(x)$
11	11	0.300	0.102			0.031
11	12	0.670	0.197	1	0.670	0.132
12	12	0.030	0.095			0.003
				$\Pr(Q = S)$	0.670	
				$\Pr(Q = R)$		0.165
				LR		4.054

(b)

		Genotype probability distributions			Match probabilities	
Allele pair		Q'	R	S	$\Pr(Q' = S)$	$\Pr(Q' = R)$
x		$q\prime(x)$	$r(x)$	$s(x)$	$q\prime(x) \cdot s(x)$	$q\prime(x) \cdot r(x)$
11	11	0.333	0.102			0.034
11	12	0.333	0.197	1	0.333	0.066
12	12	0.333	0.095			0.032
				$\Pr(Q' = S)$	0.333	
				$\Pr(Q' = R)$		0.131
				LR		2.539

Curran discussed the genotype ambiguity of STR locus D13S317 on this data set, so we illustrate the MLR approach on his inferred genotype Q at this locus. Proceeding from left to right (Table 2a), the first table column gives the allele pair genotype values that appear in the posterior distribution. Column $q(x)$ shows the posterior probability values of genotype Q at D13S317, column $r(x)$ shows the population probabilities of genotype R and column $s(x)$ shows the unambiguous suspect genotype S with allele pair [11, 12]. Each term in the numerator match probability $\Pr\{Q = S\}$ appears in column $q(x) \cdot s(x)$, which sums to 0.670. The terms in the denominator match probability $\Pr\{Q = R\}$ appear in column $q(x) \cdot r(x)$; these add up to 0.165. The LR is the ratio of these two match probabilities, which equals 4.054. The weight of evidence (base 10 logarithm of the LR) information at D13S317 with genotype Q is therefore 0.608.

Alternatively, a maximizing approach can produce a genotype Q' from the list of allele pairs contained in D13S317's 99% highest posterior probability set.[2] By considering each allele pair in this unordered set to be equally likely, we form a new genotype Q' that has the uniform probabilities shown in column $q'(x)$ (Table 2b). Columns $r(x)$ and $s(x)$ are unchanged from Table 2a. Assessing the MLR of Q' relative to that of genotype Q, the numerator match probability $\Pr\{Q' = S\}$ is halved

[2] One might instead consider using a single maximum probability allele pair value. However, making such a definite genotype value assignment risks producing an entirely uninformative joint LR of zero when a misclassification occurs (Cowell *et al.*, 2007).

TABLE 3 *The LR and log(LR) values are shown at every locus for inferred genotypes Q and Q′. The joint weight of evidence is the sum of the locus log(LR) values*

Locus	LR		Log (LR)	
	Q	Q'	Q	Q'
CSF1PO	3.089	1.658	0.490	0.220
D13S317	4.054	2.539	0.608	0.405
D16S539	10.962	5.006	1.040	0.699
D18S51	30.640	5.310	1.486	0.725
D21S11	11.951	4.485	1.077	0.685
D3S1358	11.901	3.712	1.076	0.570
D5S818	7.668	4.000	0.885	0.602
D7S820	10.172	3.603	1.007	0.557
D8S1179	111.981	4.034	2.049	0.606
FGA	14.732	5.553	1.168	0.745
TH01	68.311	17.566	1.834	1.245
TPOX	21.507	2.984	1.333	0.475
vWA	50.046	14.552	1.699	1.163
		Joint log (LR)	15.753	8.695

to 0.333, and the denominator match probability $\Pr\{Q' = R\}$ is the slightly smaller 0.131. The LR for uniform genotype Q' is reduced to 2.539, with a lower logarithmic information value of 0.405.

We compared the LRs and $\log_{10}$(LR)s of inferred genotypes Q and Q' (Table 3). At every locus, the posterior distribution genotype Q (unequal inferred $q(x)$ probabilities) has a more informative LR than the uniform genotype Q' (equal $q'(x)$ probabilities). By the product rule (i.e. locus independence), the joint LR for Q is $10^{15.75}$, whereas the joint LR for Q' is $10^{8.70}$. The reason for this seven order of magnitude LR improvement is that the full posterior genotype pmf inferred from the quantitative data is more informative than a set of equally probable allele pairs.

7. Computational considerations

The MLR approach decomposes the LR computation into two steps (Figure 1a). The first step sums over every genotype possibility x in the context of the evidence data (and other parameters) using Bayes theorem to infer a posterior probability distribution $q(x)$ for genotype Q. Then, MLR combines the three genotypes Q, R and S by summing over the products of their probability distributions to form the LR. The conventional DLR instead computes the LR in a single step (for both numerator and denominator) that sums over genotype values (Evett *et al.*, 1998) (Figure 1b). That is, the MLR uses an explicit genotype representation Q that has been partially evaluated (Futamura, 1971) from these data, whereas the DLR does not preserve a genotype object in an intermediate step.

There can be conceptual utility in forming and preserving the genotype Q and its probability function $q(x)$. The genotype is a natural representation of genetic identity since it corresponds directly to an individual's DNA type. Also, its probability distribution captures our knowledge (and uncertainty) about unknown allele pair values. Some people find it helpful to visualize genotype

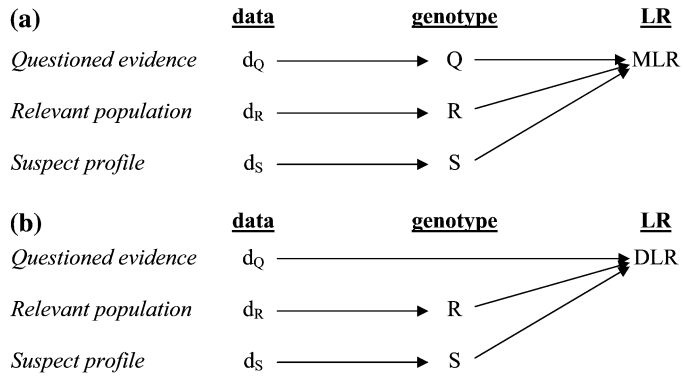

FIG. 1. (a) The MLR is computed from three genotypes, each of which is inferred independently from their respective data. (b) The DLR is computed by summing over all genotype possibilities for the questioned evidence and does not use a posterior genotype pmf Q. While both approaches use a likelihood function to compare genotypes with data, with MLR this comparison is done when inferring a genotype pmf, while with DLR this is done through genotype summation.

value combinations (e.g. DNA mixtures) and compare these patterns with the observed data. Pedagogically, we often use these genotype concepts and pictures when educating students, judges and juries. Importantly, though, explicit representation of genotypes (as random variables) can confer significant computational advantages in certain situations.

Genotype inference can be computationally expensive when using a faithful hierarchical Bayesian model that accurately accounts for quantitative STR peak data. The associated genotype MCMC summation (and integration over other variables) for DNA mixture problems typically entails hours or days of computer time (Perlin, 2005; Cowell *et al.*, 2008; Curran, 2008). With the DLR, this genotype summation cost is incurred anew every time a comparison is made with a different suspect genotype S. However, the MLR approach exacts this cost only once since the evidence genotype Q is preserved. The inferred pmf $q(x)$ can therefore be reused in each subsequent (virtually instantaneous sum of products) suspect comparison.

DNA databases enable 'cold hit' comparisons between crime scene evidence and suspect genotypes. Providing a LR score for every scene-to-suspect match can quantify database match information. The most informative LR is obtained when modelling the original quantitative peak height evidence (Balding and Buckleton, 2009), which can be preserved for the ith case in an MCMC inferred genotype Q_i having Bayesian pmf $q_i(x)$. Comparing the stored scene genotype Q_i with a set of J suspect genotypes $\{S_j\}$ is a very fast computation using MLR equation (5). However, the DLR computation does not preserve any genotype Q_i, so its costly MCMC integration must be repeated J times over the same case i quantitative data, once for each suspect j. While MLR naturally supports highly informative DNA database LR determination (Perlin, 2005), a redundant DLR approach would be computationally prohibitive for typical database sizes (e.g. where J is a million or more convicted offenders).

When identifying victim remains in a mass disaster, there can be uncertainty in both the victim remains genotypes $\{Q_i\}$ and the missing person genotypes $\{S_j\}$. In our work on reanalysing the World Trade Center (WTC) disaster DNA data (Perlin, 2007), each of the I genotypes Q_i was typically inferred by a joint Bayesian analysis of data d_{Q_i}, comprising multiple samples from damaged

remains. Similarly, a subject genotype S_j could be inferred from data d_{S_j}, comprising low-level DNA or mixture personal effect samples and kinship family references. Whereas a full DLR comparison of all victim remains data $\{d_{Q_i}\}$ with all missing person data $\{d_{S_j}\}$ would entail $I \cdot J$ (multiplicative) LR computations, our MLR approach to the WTC reanalysis involved only $I + J$ (additive) genotype inferences that were afterwards compared rapidly using MLR equation (5) to obtain the LRs. Moreover, the cost of the MCMC inference was reduced since DLR's joint consideration of the d_{Q_i} and d_{S_j} data (e.g. by generalizing the quantitative data LR; Evett *et al.*, 1998, equation 5) is a more computationally expensive integration than MLR's separate inferences of genotype Q_i from just data d_{Q_i} and of genotype S_j from just data d_{S_j}.

8. Court case

The likelihood component of a total probability model describes how well the model accounts for observed data. A more accurate likelihood function can elicit greater identification information from the data (Gill *et al.*, 2006), hence infer a more informative genotype pmf. In Bayesian inference (O'Hagan and Forster, 2004), complete modelling of the quantitative data can infer a genotype that preserves all of the data's identification information. The MLR provides a mechanism for automatically translating this evidence genotype (probability) representation into a LR, when making a comparison with a suspect relative to a population. We recently served as scientific experts in a criminal trial[3] that highlighted several points along the information spectrum of (infinitely many possible) likelihood functions and demonstrated how MLR can help explain match information in court.

Dentist John Yelenic was murdered in his home in Southwestern Pennsylvania. Pennsylvania State Trooper Kevin Foley, cohabitating boyfriend of the victim's estranged wife, was accused of the homicide. The primary physical evidence was a two-person DNA mixture extracted from the victim's fingernails, containing the victim (93% of total DNA) and a second minor unknown contributor (7%). Interpreting the mixture evidence using an inclusion method to determine PI, the original Federal Bureau of Investigation laboratory reported a DNA match statistic LR_{PI} of 13 000, considerably less than the million to one level that juries find persuasive (Koehler, 2001). The prosecution therefore retained independent outside experts (Drs Cotton and Perlin) to perform more informative interpretations of the DNA mixture evidence.

Dr Cotton's obligate allele (OA) analysis listed all allele pairs at a locus that contained an evidence allele other than the victim's, yielding a LR_{OA} of 23 million. Dr Perlin conducted a quantitative modelling (QM) of the mixture data using Cybergenetics TrueAllele® computer system, finding a LR_{QM} of 189 billion. TrueAllele genotype inference uses MCMC to explore a Bayesian model (Perlin, 2003) with a multivariate normal (peak height) data likelihood function (Perlin and Szabady, 2001) and generally accepted hierarchical mixture weight modelling (Curran, 2008) with additional variables for stutter (Perlin *et al.*, 1995) and relative amplification (Ng, 1998) polymerase chain reaction (PCR) artifacts. Unlike the original laboratory's PI approach, the OA and QM methods both assumed that the victim contributed DNA to his own fingernail sample (observed in the data as a 93% major component). In all three methods, LR comparison was made to suspect Foley, relative to a Caucasian reference population (Budowle *et al.*, 1999).

The judge admitted the OA and QM methods into evidence after hearing the outside experts testify on the general acceptance of these LR approaches in the relevant scientific community of

[3] *Commonwealth of Pennsylvania* v. *Kevin J. Foley*, Indiana County, No. 1170, Crim 2009.

forensic inference and statistics. At the trial, the defense cross-examination questions focused on why there were three different DNA match statistics (LR_{PI}, LR_{OA} and LR_{QM}) having very different magnitudes (10^4, 10^7 and 10^{11}) for the same data. The prosecution experts compared genotype patterns with peak data to educate the jury about DNA mixture interpretation. Each interpretation method used progressively increasing amounts of the data to infer a genotype pmf:

- PI did not use either the victim profile or the quantitative peak heights;
- OA did use the victim profile, but not peak heights; and
- QM used both the victim profile and the quantitative data.

The experts explained that using more of the data generally produces a more informative genotype.

MLR is a natural way to translate genotype possibilities (relative to a suspect and a population) into LR match information. We explained to the jury that (the MLR formulation of) the LR is the probability of a specific match between genotypes Q and S, relative to that of a random match between Q and R. Using a spreadsheet that presented the MLR calculation (similar to Table 2), the jurors saw how multiplying, adding and dividing genotype pmfs would compute a LR at a locus. We presented the LR contribution at each locus, comparing the three interpretation methods (analogous to Table 3); this bar chart showed how more informative genotypes produced a higher LR at certain loci. We gave the plain English statement of the LR (see MLR equation (4) paragraph), which does not mention conditional probabilities and can be applied equally well to all three methods. Although Trooper Foley testified that he was innocent, the DNA fingernail evidence indicated otherwise. The jury convicted him of first-degree murder.

9. Discussion

We have introduced a LR approach for inferring match strength when there are uncertain genotypes. The key idea is to form a LR that compares the probability of a specific genotype match relative to that of a nonspecific match. The MLR assesses identification hypotheses for an observed match event, which works well with posterior genotype probability distributions, and provides information that is equivalent to the usual data event DLR. The MLR preserves the data's identification information by using the entire posterior genotype probability distribution rather than a limited subset.

Much of the power of DNA evidence comes from making cold hit comparisons to offender databases (Gill and Werrett, 1990; Niezgoda and Brown, 1995). These databases compare a set of evidence genotypes $\{Q_i\}$ with a set of likely suspect genotypes $\{S_j\}$. In particular, comparisons are made between genotypes, without any use of the underlying genetic data. The MLR supports this DNA database paradigm by working directly with (possibly uncertain) genotypes and efficiently computing a LR weight of evidence for every reported match.

The MLR transforms an inferred questioned evidence genotype (along with suspect and population genotypes) into a single information measurement number. This summarization is useful for validating a genotype inference method (or a laboratory procedure) since the observed LR distribution can characterize the information efficacy (distribution mean) and reproducibility (within-case variance) (Perlin, 2006). Similarly, the information yield of different DNA laboratory and genotype inference methods can be compared through their LR values on representative specimens. When reporting a DNA match, the MLR summarizes identification rarity, preserving all of the data information contained in the posterior genotype pmf.

To reduce examiner bias, an objective approach is to (i) first infer (and commit to) a questioned genotype from the evidence data, (ii) only afterwards make any match comparison with a suspect genotype and (iii) then report a LR rarity statistic with respect to a relevant population (Berry, 1991; Tobin and Thompson, 2006). The MLR supports this inference sequence since (4) can compare any questioned genotype Q with any suspect genotype S and determine the LR with respect to a population genotype R. Indeed, the MLR is able to 'match' DNA materials only after all the genotypes Q, R and S have been determined.

There are many genotype inference methods for mixtures and other complex DNA data. The genotypes that result from applying these diverse methods to the same data can produce LR match information ranging over 10 orders of magnitude (Butler and Kline, 2005). Statistical computing infers genotypes that tend to preserve more identification information and provide greater consistency. The MLR can accept genotype input that has been inferred using any of these methods and preserve all of the match information contained in the genotype pmf.

The MLR accommodates ongoing scientific improvements in genotype inference. Hierarchical Bayesian modelling can be continuously refined to incorporate more aspects of the STR data process and its uncertainty (e.g. PCR stutter, relative amplification, degraded DNA, marker balance, many unknown contributors, low-level DNA). Moreover, a model can combine independent DNA sample data using a joint likelihood function that multiplies together the separate likelihoods, as we routinely do in the TrueAllele system with low-level DNA mixtures. Regardless of the model specification, the inferred output is a genotype pmf that can be easily compared with other genotypes using MLR.

The MLR approach has application beyond DNA evidence. The Bayesian framework of first inferring a type, and then using the type's pmf in MLR equation (5) to compute a match rarity LR, is entirely general. We have mapped this framework onto other forensic subdisciplines, such as fire debris, firearms/toolmarks, blood spatter and fingerprints. For example, using integrals in place of sums, one can derive the standard LR formula for glass evidence (Lindley, 1977) as a MLR of normally distributed types.

Forensic science has been criticized for lacking a sound statistical basis for reporting matches and their rarity (National Research Council, 2009). While DNA evidence has been relatively unscathed, the continuing debate over DNA mixture interpretation (Gill *et al.*, 2006; Budowle *et al.*, 2009c) and low-level DNA (Balding and Buckleton, 2009; Budowle *et al.*, 2009b) shows that DNA is not entirely immune to such challenges. Some have proposed that it is not even possible to give other non-DNA subdisciplines a rigorous statistical basis (Budowle *et al.*, 2009a). The MLR framework suggests otherwise. Bayesian inference permits the probabilistic inference of forensic types, and MLR enables their comparison to ascertain match rarity.

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