Module 9: Statistical Approaches (RMP, CPI, LR) ISHI 2010 Mixture Workshop

Statistical Approaches (CPI, LR, RMP)

Michael D. Coble

Outline for Statistical Approaches

- **GUIDELINES**
  - SWGDAM Guidelines Section 4 – Statistical Analysis.
  - SWGDAM Guidelines Section 5 – Statistical Formulae.
  - Table 1.

- **PRINCIPLES**
  - Developing the framework to perform the appropriate statistical analyses (RMP, LR, CPI) given the mixture profile.

- **PROTOCOLS**
  - Documentation of the procedures.

- **PRACTICE**
  - Worked Example.

Steps in DNA Interpretation

http://www.cstl.nist.gov/biotech/strbase/training.htm
**Statistical Analysis of DNA Typing Results**

- 4.1. The laboratory must perform statistical analysis in support of any inclusion that is determined to be relevant in the context of a case, irrespective of the number of alleles detected and the quantitative value of the statistical analysis.

Buckleton & Curran (2008): “There is a considerable aura to DNA evidence. Because of this aura it is vital that weak evidence is correctly represented as weak or not presented at all.”

**Comparison of DNA Typing Results**

- 3.6.1. The laboratory must establish guidelines to ensure that, to the extent possible, DNA typing results from evidentiary samples are interpreted before comparison with any known samples, other than those of assumed contributors.

**Comparison of DNA Typing Results**

- 3.6.2. DNA typing results may not be obtained at all loci for a given evidentiary sample (e.g., due to DNA degradation, inhibition of amplification and/or low-template quantity); a partial profile thus results.

- 3.6.2.1. For partial profiles, the determination of which alleles/loci are suitable for comparison and statistical analysis should be made prior to comparison to the known profiles.

**Principles**

Schneider et al. (2009) and SWGDAM

- Not all mixtures are homogeneous for Types A, B and C e.g. Predominantly “A” with some “B” and “C” loci

**Guidelines**

Do you classify mixtures using a scheme like the German Stain Commission?

1. Yes
2. No
3. Sometimes for difficult or low level samples.
4. I use CPE or CPI stats, so a mixture is a mixture to me.

**Guidelines**

Comparison of DNA Typing Results

SWGDAM Guideline 3.6 (Intro):

- The following determinations can be made upon comparison of evidentiary and known DNA typing results (and between evidentiary samples):
  - The known individual cannot be excluded (i.e., is included) as a possible contributor to the DNA obtained from an evidentiary item.
  - The known individual is excluded as a possible contributor.
  - The DNA typing results are inconclusive/uninterpretable.
  - The DNA typing results from multiple evidentiary items are consistent or inconsistent with originating from a common source(s).
**GUIDELINES**

Statistical Analysis of DNA Typing Results

- 4.1. The laboratory must perform statistical analysis in support of any inclusion.
- 4.2. For calculating the CPE or RMP, any DNA typing results used for statistical analysis **must be** derived from **evidentiary items** and not known samples.
- 4.3. The laboratory must not use inconclusive/uninterpretable data (e.g., at individual loci or an entire multi-locus profile) in statistical analysis.

**GUIDELINES**

Statistical Analysis of DNA Typing Results

- 4.4. Exclusionary conclusions do not require statistical analysis.
- 4.5. The laboratory must document the source of the population database(s) used in any statistical analysis.

**PRINCIPLES**

Statistical Approaches with Mixtures

- **Random Match Probability (RMP)** – The major and minor components can be successfully separated into individual profiles. A random match probability is calculated on the evidence as if the component was from a single source sample.

\[
RMP_{\text{major}} = 2pq
\]

**PRINCIPLES**

Statistical Approaches with Mixtures

- **Random Man Not Excluded (CPE/CPI)** - The probability that a random person (unrelated individual) would be excluded as a contributor to the observed DNA mixture.

\[
p = f(a) + f(b) + f(c) + f(d) \\
q = 1 - p \\
PE = 2pq + q^2 \\
CPE = P_{E|H_1} \times P_{E|H_2} \cdots \\
CPI = 1 - CPE \\
\]

**PRINCIPLES**

Statistical Approaches with Mixtures

- **Likelihood Ratio** - Comparing the probability of observing the mixture data under two (or more) alternative hypotheses; in its simplest form \( LR = 1/RMP \)

\[
P(E|H_1) \\
= \frac{1}{2pq} \\
P(E|H_2) \\
= \frac{1}{2pq} = 1/RMP \\
\]

**PRINCIPLES**

Statistical Approaches with Mixtures

Do you interpret your evidence (lock down your inferred genotypes) independent of your alleged contributor?

1. Always
2. Most of the time
3. Sometimes
4. Rarely
5. Never

http://www.cstl.nist.gov/biotech/strbase/training.htm
Principles

Statistical Approaches with Mixtures

- **Unrestricted Likelihood Ratio** - All combinations of alleles are deemed possible (relative peak height differences are not utilized).

  ![Possible Combinations](a b c d)

  \[ \text{Possible Combinations} = (\text{AB + AC + AD + BC + BD + CD}) \]

- **Restricted Likelihood Ratio** - Based on relative peak heights, alleles are paired only where specific combinations of alleles are deemed possible.

  ![Possible Combinations](a b c d)

  \[ (\text{without victim subtraction}) = (\text{AD + BC}) \]

  \[ 2pq + 2pq \]

Summary

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<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>RMNE (CPI, CPE)</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Random Match Prob,</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Restricted LR</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Unrestricted LR</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
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Advantages and Disadvantages

**RMNE (CPI/CPE)**

- **Advantages**
  - Does not require an assumption of the number of contributors to a mixture
  - Easier to explain in court

- **Disadvantages**
  - Weaker use of the available information (robs the evidence of its true probative power because this approach does not consider the suspect’s genotype)
  - LR approaches are developed within a consistent logical framework

**Likelihood Ratios (LR)**

- **Advantages**
  - Enables full use of the data including different suspects

- **Disadvantages**
  - More difficult to calculate (software programs can assist)
  - More difficult to present in court

Summary

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What kind of mixture statistic(s) does your lab use?

1. LR
2. CPE (RMNE, CPE)
3. RMP
4. CPE or RMP
5. Other combinations
6. Probabilistic modeling (e.g., TrueAllele)
7. We don’t use stats (contradicting the new guidelines – section 4.1)
8. Don’t get all mathy on me.

Does your lab use any software to help calculate mixture stats?

1. PopStats
2. GMID-X
3. FSS
4. GeneMarker HID
5. True Allele
6. DNA-View
7. In-house Excel program
8. On a calculator (painfully)
9. Other
Assumptions for CPE/CPI Approach

- **There is no allele dropout** (i.e., all alleles are above stochastic threshold) – low-level mixtures can not reliably be treated with CPE
- All contributors are from the same racial group (i.e., you use the same allele frequencies for the calculations)
- All contributors are unrelated
- Peak height differences between various components are irrelevant (i.e., component deconvolution not needed) – this may not convey all information from the available sample data...

Statistical Analysis of DNA Typing Results

4.6.3. When using CPE/CPI (with no assumptions of number of contributors) to calculate the probability that a randomly selected person would be excluded/included as a contributor to the mixture, loci with alleles below the stochastic threshold may not be used for statistical purposes to support an inclusion. In these instances, the potential for allelic dropout raises the possibility of contributors having genotypes not encompassed by the interpreted alleles.

CPI vs. LR

Vaginal Swab

ST = 150 RFU

PRINCIPLES

Curran and Buckleton (2010)

Included Probabilities and Dropout

Creating 1000 Two-person Mixtures (Budowle et al. 1999 AFm freq.).

Created 10,000 "third person" genotypes.

Compared "third person" to mixture data, calculated PI for included loci, ignored discordant alleles.

"the risk of producing apparently strong evidence against an innocent suspect by this approach was not negligible."

"It is false to think that omitting a locus is conservative as this is only true if the locus does not have some exclusionary weight."

http://www.cstl.nist.gov/biotech/strbase/training.htm
CPI vs. LR

Restricted LR

Assume two person mixture

Victim – 23, 24

ST = 150 RFU

\[
\frac{P(E|H_1)}{P(E|H_2)} = \frac{V + S}{V + U} = \frac{2(f_{23})(f_{24}) + 1}{2(f_{23})(f_{24}) + 2(f_{17})(f_{21})}
\]

LR = 1/2(f_{17})(f_{21})

LR = 1/2(0.1941)(0.0197) = 130.76

Combined LR = 333.34

CPI vs. LR

Restricted LR

Assume two person mixture

Victim – 12, 12

ST = 150 RFU

Conclusion

Combined LR = 43,587

Suitable Statistical Analyses

Table 1 – Suitable Statistical Analyses for DNA Typing Results

<table>
<thead>
<tr>
<th>Category of DNA Typing Result</th>
<th>RMP</th>
<th>CPI/CPI</th>
<th>LR (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Source</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Single Major Contributor to a Mixture</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Multiple Major Contributors to a Mixture</td>
<td>✓ (2)</td>
<td>✓ (2)</td>
<td></td>
</tr>
<tr>
<td>Single Minor Contributor to a Mixture</td>
<td>✓</td>
<td>✓ (3)</td>
<td></td>
</tr>
<tr>
<td>Multiple Minor Contributors to a Mixture</td>
<td>✓ (2)</td>
<td>✓ (3)</td>
<td></td>
</tr>
<tr>
<td>Indistinguishable Mixture</td>
<td>✓ (1)</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

1. Restricted or unrestricted
2. Restricted
3. All potential alleles identified during interpretation are included in the statistical calculation

Summary

- The laboratory must perform statistical analysis in support of any inclusion (4.1).
- DNA typing results from evidentiary samples are interpreted before comparison with any known samples, other than those of assumed contributors (3.6.1).
- There are advantages and disadvantages to both RMNE and LR stats. As a general rule, RMNE does not take full advantage of all the data.
- Statistical methods cannot be combined into one calculation (e.g. combining RMP at one locus with a CPI calculation at a second locus is not appropriate).

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