Perspectives on the Future: What We Have Learned and Where We Need to Go

John M. Butler

October 15, 2012
Nashville, TN
Comments on Mixture Training We Have Conducted These Past Two Years

- Trying to help analysts better understand the SWGDAM 2010 Interpretation Guidelines
  - It is important to note that the 2010 SWGDAM Guidelines were written primarily for 2-person mixtures situations

- However, many labs are doing or attempting more complex mixtures often without appropriate underlying validation support or consideration of complicating factors

- The information content in our workshops has continued to evolve to include the latest published articles…
If you want to be a technician, performing tests on requests, then just focus on the policies and procedures of your laboratory. **If you want to be a scientist and a professional**, learn the policies and procedures, but go much further and learn the philosophy of your profession. **Understand the importance of why things are done** the way they are done, the scientific method, the viewpoint of the critiques, the issues of bias and the importance of ethics.
My Goals in This Presentation

• Valuable mixture literature and how to obtain it

• Important lessons & common misunderstandings

• Thoughts on where we need to go as a community to improve mixture interpretation
Feedback from a Previous Workshop

Which of the topics below would be your first choice for additional training?

1. Relevant literature
2. How to validate thresholds
3. How to develop relevant SOPs
4. Interpretation of low level mixtures
5. Statistics

From one of the regional mixture workshops (Apr – June 2011)

2/3 want more information on these topics

Relevant literature not viewed as important
Mixture Literature

you should be reading…

See DNA Mixtures Reference List provided with workshop materials
Quality Assurance Standard Requirement for Literature Review

Quality Assurance Standards for Forensic DNA Testing Laboratories
(effective September 1, 2011)

5.1.3.2. The laboratory shall have a program approved by the technical leader for the **annual review of scientific literature** that documents the analysts’ ongoing reading of scientific literature. The laboratory shall maintain or have physical or electronic access to a collection of current books, reviewed journals, or other literature applicable to DNA analysis.

How many DNA-related articles would you estimate that you read in a typical month?

1. None
2. 1 article
3. 2 to 5 articles
4. More than 5 articles
5. None, I only read the abstracts
6. I don’t make time to read!

Data from 106 responses
ISHI Mixture Workshop (Oct 2012)
Last Year’s Response

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Data from 133 responses
ISHI Mixture Workshop (Oct 2011)

73% are reading 1-5 articles per month
Importance of Reading the Literature
How can you keep up and improve?

• Develop a culture in your laboratory to read the literature and share information with one another

• Obtain access to appropriate journals
  – Join AAFS and/or ISFG
  – Develop a relationship with a local university in order to get access to the latest journal articles

• Read, Think, and Implement Improvements!
Useful Articles on DNA Mixture Interpretation


Read to Maintain a Big Picture View!

If you are not following the recent literature, you would have missed:

- Software applications & implementation
- Impact of allele dropout on stats
- Studies on number of contributors

- The literature is changing very fast
  - Read more than *Journal of Forensic Sciences* to stay caught up

- **Make time in your schedule to read and ask critical questions**
### Number of Articles Published on DNA and DNA Mixtures

PubMed.gov search conducted September 14, 2012 using “DNA” or “DNA mixtures” and journal name with and without “and 2012”

<table>
<thead>
<tr>
<th>Journal Name</th>
<th>“DNA”</th>
<th>“DNA mixtures”</th>
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<td>Int. J. Legal Med.</td>
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<td>Science &amp; Justice</td>
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<td>Mixture Principles &amp; Recommendations</td>
<td>13</td>
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<tr>
<td>Setting Thresholds</td>
<td>11</td>
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<tr>
<td>Stutter Products &amp; Peak Height Ratios</td>
<td>19</td>
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<td>Stochastic Effects &amp; Allele Dropout</td>
<td>18</td>
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<td>Estimating the Number of Contributors</td>
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<td>Mixture Ratios</td>
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<tr>
<td>Statistical Approaches</td>
<td>23</td>
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<tr>
<td>Low Template DNA Mixtures</td>
<td>8</td>
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<tr>
<td>Separating Cells to Avoid Mixtures</td>
<td>3</td>
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<tr>
<td>Software (plus 12 websites)</td>
<td>7</td>
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<tr>
<td>Probabilistic Genotyping Approach</td>
<td>11</td>
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<tr>
<td>General Information on Mixtures</td>
<td>7</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>144</strong></td>
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Will be regularly updated on [http://www.cstl.nist.gov/strbase/mixture.htm](http://www.cstl.nist.gov/strbase/mixture.htm)

7/8 in the past year; mostly in *FSI Genetics*
Recent articles on mixtures not found in JFS…
DNA commission of the International Society of Forensic Genetics: Recommendations on the evaluation of STR typing results that may include drop-out and/or drop-in using probabilistic methods

P. Gill\textsuperscript{a,b,*}, L. Gusmão\textsuperscript{c}, H. Haned\textsuperscript{d}, W.R. Mayr\textsuperscript{e}, N. Morling\textsuperscript{f}, W. Parson\textsuperscript{g}, L. Prieto\textsuperscript{h}, M. Prinz\textsuperscript{i}, H. Schneider\textsuperscript{j}, P.M. Schneider\textsuperscript{k}, B.S. Weir\textsuperscript{l}

\textsuperscript{a} Norwegian Institute of Public Health, Oslo, Norway
\textsuperscript{b} University of Oslo, Oslo, Norway
\textsuperscript{c} IPATIMUP, Institute of Molecular Pathology and Immunology of the University of Porto, Portugal
\textsuperscript{d} Netherlands Forensic Institute, Department of Human Biological Traces, The Hague, The Netherlands
\textsuperscript{e} Department of Blood Group Serology and Transfusion Medicine, Medical University of Vienna, Austria
\textsuperscript{f} Section of Forensic Genetics, Department of Forensic Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
\textsuperscript{g} Institute of Legal Medicine, Innsbruck Medical University, Innsbruck, Austria
\textsuperscript{h} Comisaría General de Policía Científica, University Institute of Research in Forensic Sciences (IUICP), Madrid, Spain
\textsuperscript{i} Office of the Chief Medical Examiner, Department of Forensic Biology, New York, USA
\textsuperscript{j} Hessisches Landeskriminalamt, Wiesbaden, Germany
\textsuperscript{k} Institute of Legal Medicine, Faculty of Medicine, University of Cologne, Germany
\textsuperscript{l} University of Washington, Department of Biostatistics, Seattle, USA
Elsevier Journal Package
Available with AAFS Membership

For ~$100 per year, you obtain electronic access to:

- Forensic Sci Int: Genetics
- Forensic Sci Int
- Science & Justice
- Legal Medicine
- Forensic & Legal Medicine

http://www.sciencedirect.com/forpac
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Individual Membership
You can apply for membership by using the Online Application Form. Please state your field of expertise in forensic genetics, and give the name of two members of the ISFG willing to support your membership. You need a valid E-mail address for verification of your application.

Please note that you will receive the confirmation of your membership by email. Together with this mail, you will receive information about the payment of membership fees (at present EUR 60.00 per year). The membership fee includes access to the congress proceedings Progress in Forensic Genetics, published online every other year after the ISFG conference.

In addition, all ISFG members receive a complimentary subscription (print and online version) of the scientific journal Forensic Science International: Genetics which is published in affiliation with our society.
Abstracts are Freely Available on Website

http://www.fsiigenetics.com/
FSI Genetics Supplement Series
Articles are Freely Available

Articles (2-3 pages each) covering presentations given at the ISFG meetings every two years

http://www.fsigeneticssup.com

2011: 281 articles
2009: 253 articles
2007: 272 articles
Know the Literature

• Sometimes articles may not be all that they claim to be – evaluate them critically

• Stay informed in order to be a good scientist

• Mixtures Using SOUND Statistics, Interpretation, and Conclusions involves knowing the literature (past and present)
Important Lessons

• People think they understand the basics of interpretation better than they actually do – this is what leads to observed variation in interpreting mixtures…

• Increased complexity of mixtures (with more allele sharing) leads to higher uncertainty which leads to lack of confidence in potential contributor genotypes

• Worked examples are beneficial in training (participants need to work through the examples themselves)

• There is value in using a profile interpretation worksheet to document assumptions and decisions made
Make decisions on the evidentiary sample and document them prior to looking at the known(s) for comparison purposes.
Steps in DNA Interpretation

- **Question sample**
- **Known sample**

### Steps:

1. **Peak** (vs. noise)
2. **Allele** (vs. artifact)
3. **Genotype** (allele pairing)
4. **Profile** (genotype combining)

### Mixture

- Weight of Evidence
- Match probability

**It’s the potential Genotypes NOT the Alleles that matter in mixtures!**
Common Misunderstandings

• Using CPI stats is conservative to the defendant
  – The numerical stat is low but by throwing out information
    the ability to EXCLUDE innocent people is reduced

• Using CPI stats means that the potential number of
  contributors is not important
  – Higher numbers of contributors dilutes out the amount of
    DNA for each contributor which leads to more stochastic
    effects and the possibility of allele dropout (more
    uncertainty)
  – The CPI stat cannot handle allele dropout!
Handling Complex Mixtures

• Stochastic thresholds are necessary in combination with CPI statistics but may not apply for >2 person mixtures (due to potential allele sharing)

• Most labs are not adequately equipped to cope with complex mixtures
  – Extrapolating validation studies from simple mixtures will not be enough to create appropriate interpretation SOPs

David Balding (UK professor of statistical genetics): “LTDNA cases are coming to court with limited abilities for sound interpretation.” (Rome, April 2012 meeting)
Thoughts on Where We Need to Go

• Away from CPI and towards likelihood ratio approaches
  – As noted in the Gill et al. (2006) ISFG DNA Commission recommendation #2

• This will require software to perform the calculations
  – This software will need to be validated
  – Peter Gill and others in Europe are pushing freeware solutions

• Still will require analysts to understand what is going on in the computer calculations!
  – Will require more significant engagement in mixture training

• The U.S. will be moving to more STR loci in the near future (from 13 to ~20 core STRs)
  – Using loci with better powers of discrimination will be helpful
Thank you for your attention

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Contact Information

John Butler
NIST Fellow
Group Leader of Applied Genetics
john.butler@nist.gov
301-975-4049

http://www.cstl.nist.gov/biotech/strbase

Our team publications and presentations are available at:
http://www.cstl.nist.gov/biotech/strbase/NISTpub.htm