NIST National Institute of Standards and Technology U.S. Department of Commerce

Mixture Interpretation using Probabilistic Genotyping

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Statistical Analysis of DNA Typing Results

SWGDAM Guidelines 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**."

Buckleton, J. and Curran, J. (2008) A discussion of the merits of random man not excluded and likelihood ratios. *Forensic Sci. Int. Genet.* 2: 343-348.

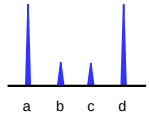
Statistical Approaches with Mixtures

See Ladd *et al.* (2001) *Croat Med J.* 42:244-246

"Exclusionary" Approach	"Inferred Genotype" Approach
Random Man Not Excluded (RMNE)	**Random Match Probability (RMP)**
Combined Prob. of Inclusion (CPI)	**(mRMP)**
Combined Prob. of Exclusion (CPE)	**Likelihood Ratio (LR)**

Statistical Approaches with Mixtures

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



$$CPI = (f(a) + f(b) + f(c) + f(d))^2$$

$$CPI = PI_{M1} \times PI_{M2} \cdots$$

$$CPE = 1 - CPI$$

"Advantages and Disadvantages" RMNE

RMNE (CPE/CPI)

Advantages

- Does not require an assumption of the number of contributors to a mixture
- Easier to explain in court
- Deconvolution is not necessary

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).
- Alleles below ST cannot be used for statistical purpose
- There is a potential to include a non-contributor

Summarized from John Buckleton, *Forensic DNA Evidence Interpretation*, p. 223 Buckleton and Curran (2008) *FSI-G* 343-348.

Curran and Buckleton (2010)

JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, September 2010, Vol. 55, No. 5
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Available online at: interscience.wiley.com

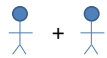
PAPER
CRIMINALISTICS; GENERAL

James M. Curran,[1] M.Sc.(Hons.), Ph.D. and John Buckleton,[2] Ph.D.

Inclusion Probabilities and Dropout

Curran and Buckleton (2010)

(1) Created 1,000
2 person mixtures



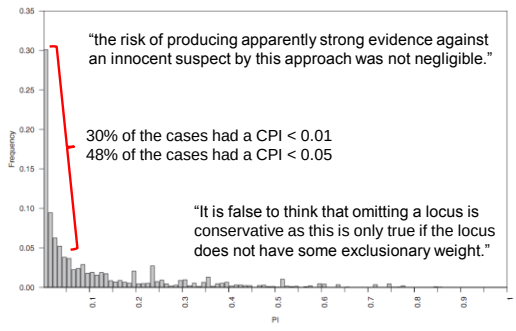
e.g. vWA 12, 15 13, 16 = 12, 13, 15, 16

(2) Created 10,000
Random genotypes

13, 15

(3) Compared "random person" to mixture data, calculated PI for included loci, ignored discordant alleles.

Curran and Buckleton (2010)



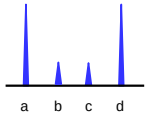
"the risk of producing apparently strong evidence against an innocent suspect by this approach was not negligible."

30% of the cases had a CPI < 0.01
48% of the cases had a CPI < 0.05

"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."

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.



$RMP_{major} = 2pq$

$= 2 \times f(a) \times f(d)$

Likelihood Ratio

ISFG Recommendations on Mixture Interpretation

http://www.isfg.org/Publication;Gill2006

1. The likelihood ratio (LR) is the preferred statistical method for mixtures over RMNE
2. Scientists should be trained in and use LRs
3. Methods to calculate LRs of mixtures are cited
4. Follow Clayton et al. (1998) guidelines when deducing component genotypes
5. Prosecution determines H_p and defense determines H_d and multiple propositions may be evaluated
6. When minor alleles are the same size as stutters of major alleles, then they are indistinguishable
7. Allele dropout to explain evidence can only be used with low signal data
8. No statistical interpretation should be performed on alleles below threshold
9. Stochastic effects limit usefulness of heterozygote balance and mixture proportion estimates with low level DNA

Gill *et al.* (2006) DNA Commission of the International Society of Forensic Genetics: Recommendations on the interpretation of mixtures. *Forensic Sci. Int.* 160: 90-101

Likelihood Ratios in Forensic DNA Work

- We evaluate the evidence (*E*) relative to alternative pairs of hypotheses
- Usually these hypotheses are formulated as follows:
  - The probability of the evidence if the crime stain originated with the suspect or Pr(*E*|*S*)
  - The probability of the evidence if the crime stain originated from an unknown, unrelated individual or Pr(*E*|*U*)

$$LR = \frac{\Pr(E \mid S)}{\Pr(E \mid U)}$$

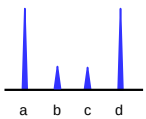
The numerator

The denominator

Slide information from Peter Gill

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



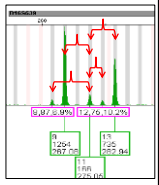
$$\frac{P(E \mid H_1)}{P(E \mid H_2)}$$

E = Evidence
H_1 = Prosecutor's Hypothesis (the suspect did it) = 1
H_2 = Defense Hypothesis (the suspect is an unknown, random person)

$$= \frac{1}{P(E \mid H_2)} = \frac{1}{2pq} = 1/\text{RMP}$$

Challenging Mixtures - Uncertainty

- **If allele dropout is a possibility** (e.g., in a partial profile), then there is uncertainty in whether or not an allele is present in the sample…and therefore what genotype combinations are possible
- **If different allele combinations are possible** in a mixture, then there is uncertainty in the genotype combinations that are possible…



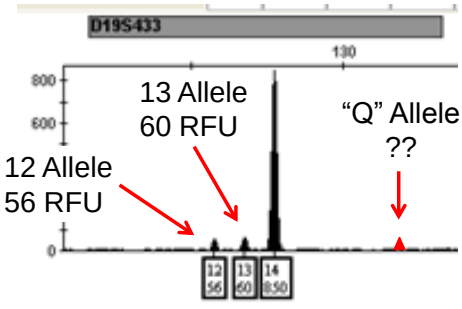
Possible allele pairing with the 11

Handling Complex Mixtures

- Stochastic thresholds are necessary in combination with CPI statistics
  - but a stochastic threshold may not hold much meaning 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

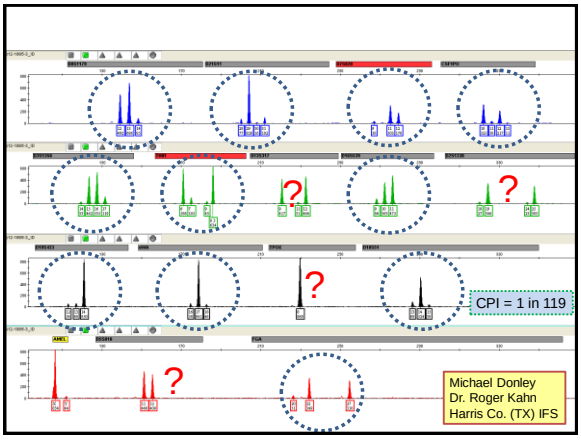
David Balding (UK professor of statistical genetics): "LTDNA cases are coming to court **with limited abilities for sound interpretation**." (Rome, April 2012 meeting)

Challenging Mixtures



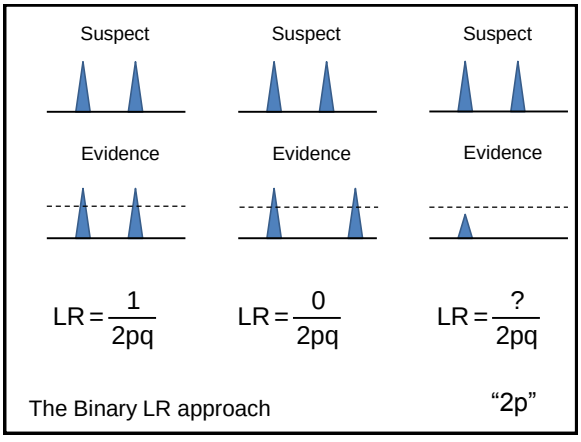
What should we do with data below our Stochastic Threshold?

- Continue to use RMNE (CPI, CPE)

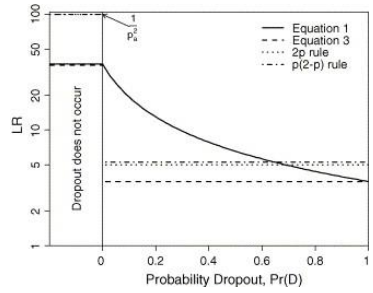


What should we do with data below our Stochastic Threshold?

- Continue to use RMNE (CPI, CPE) (not optimal)
- Use the Binary LR with 2p (not optimal)

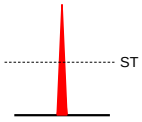


The "2p" Rule



Stain = AA

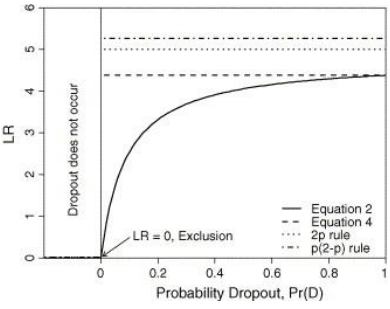
Suspect = AA



LR = 100

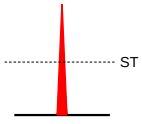
f(a) = 0.10 $1/p^2 = 100$ 1/2p = 5

The "2p" Rule



Stain = AA

Suspect = AB



Exclusion

f(a) = 0.10 1/2p = 5

Whatever way uncertainty is approached, probability is the *only* sound way to think about it.

-Dennis Lindley

Probabilistic Approaches

- "Semi-Continuous" or "Fully Continuous"
- Semi-Continuous – information is determined from the alleles present – peak heights are not considered.
- Fully Continuous – incorporation of biological parameters (PHR [Hb], Mx ratio, Stutter percentage, etc…).

What should we do with data below our Stochastic Threshold?

- Continue to use RMNE (CPI, CPE) (not optimal)
- Use the Binary LR with 2p (not optimal)
- Semi-continuous methods with a LR (Drop models)

R. v Garside and Bates

- James Garside was accused of hiring Richard Bates to kill his estranged wife, Marilyn Garside.
- Marilyn was visiting her mother when someone knocked on the door. Marilyn answered and was stabbed to death.
- A profile from the crime scene stain gave a low-level DNA profile of the perpetrator.

Summary

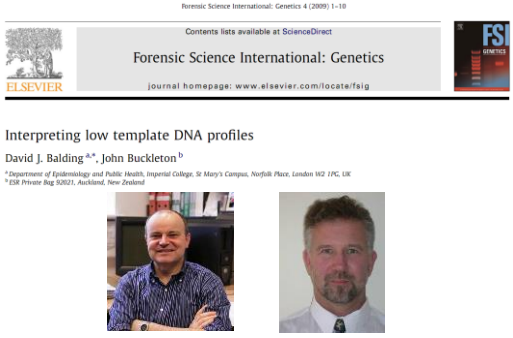
Locus	Mrs Garside	Bates	CSP: minor component
D3	16,16	13,16	13
VWA	15,17	16,16	16
D16	11,12	11,12	–
D2	20,20	**19**,22	22
D8	12,13	8,13	8
D21	30,32.2	30,31.2	31.2
D18	14,14	**12,15**	–
D19	12,14	12,15	15
THO1	9.3,9.3	7,7	7
FGA	23,25	21,21	21

Three alleles from Bates were not present in the evidence

Court case

- The Crown expert dropped the D18 locus (gave a LR = 1) from the statistical results and used "2p" for D2 to give an overall odds for Bates of 1 in 610,000.
- David Balding argued for the defense that dropping loci is not conservative.

Balding and Buckleton (2009)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journal homepage: www.elsevier.com/locate/fsig

Interpreting low template DNA profiles

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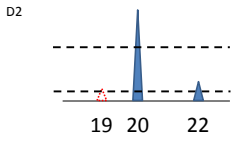
[b] ESR Private Bag 92021, Auckland, New Zealand

Present the "Drop model" for interpreting LT-DNA profiles

Drop Model



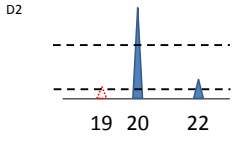
V = 20, 20
S = 19, 22
Pr(Drop-out) = 0.05
Pr(Drop-in) = 0.01

$P(E|H_1)$ = Pr(no Drop-out at 22) Pr(Drop-out at 19) Pr(No Drop-in)

= 0.95 0.05 0.99

= 0.047

Drop Model

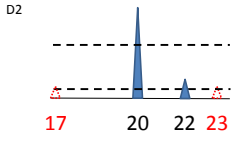


V = 20, 20
S = 19, 22
Pr(Drop-out) = 0.05
Pr(Drop-in) = 0.01

$$\frac{P(E|H_1)}{P(E|H_2)} = \frac{0.047}{}$$

The defense can now argue that someone else in the population unrelated to Bates was the true perpetrator!

Drop Model



V = 20, 20
UC = 17, 23
Pr(Drop-out) = 0.05
Pr(Drop-in) = 0.01

$P(E|H_2)$

Pr(Drop-out at 17) Pr(Drop-out at 23) Pr(Drop-in at 22)

0.05 0.05 0.01

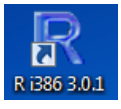
= **0.000025** x $2pq_{17,23}$ **(0.027)** = **0.000000675**

Summary

- Using "2p" for D2 gave a **LR = 11**. This is non-conservative compared to the probabilistic approach where a Pr(D) was incorporated into the calculation, the **LR = 2.8**
- The use of a probabilistic approach uses all of the information in the profile.
- The final LR in favor of the Hp was ≈ 400,000.

Software will help with the math…

Software >
likeLTD (likelihoods for low-template DNA profiles)



Evaluation of mixed-source, low-template DNA profiles in forensic science

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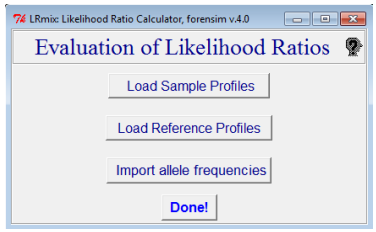
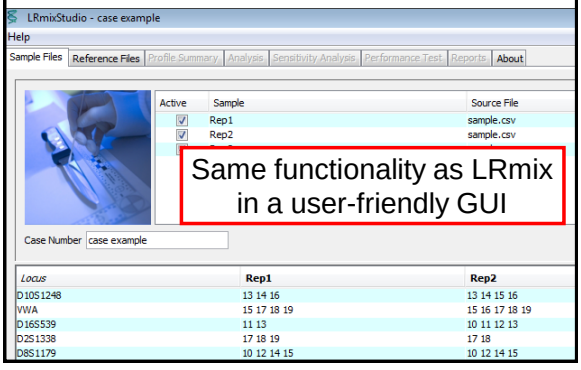
Some Semi-Continuous Examples

- LR mix (Haned and Gill)
- Balding (likeLTD - R program)
- FST (NYOCME, Mitchell *et al.*)
- Kelly *et al.* (University of Auckland, ESR)
- Lab Retriever (Lohmueller, Rudin and Inman)
- Armed Expert (NicheVision)
- Puch-Solis *et al.* (LiRa and LiRaHT)
- GenoProof Mixture (Qualitype)

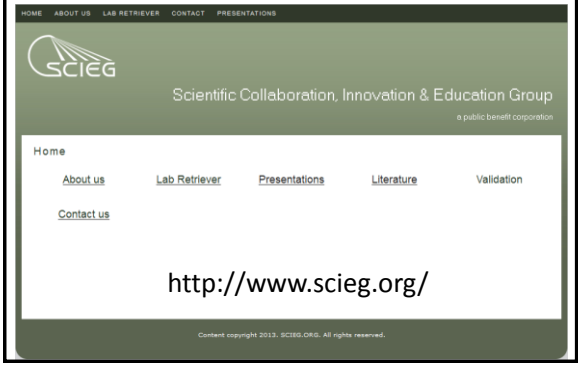
LR Mix



LRmix-Studio



Lab Retriever



Dropout Calculator

100 pg sample

Ave RFU

151.47

Kit	*Identifiler*	
Analytical Threshold	**50**	**30**
$P(D_O)$	0.059	0.006

These values are based on logistic functions generated from aggregated data of individuals

Semi-continuous methods

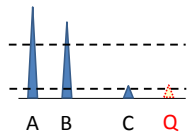
- Use a Pr(DO) and LRs
- Speed of analysis – "relatively fast"
- The methods do not make full use of data - only the alleles present.

What should we do with data below our Stochastic Threshold?

- Continue to use RMNE (CPI, CPE) (not optimal)
- Use the Binary LR with 2p (not optimal)
- Semi-continuous methods with a LR (Drop models)
- Fully continuous methods with LR

Continuous Models

- Mathematical modeling of "molecular biology" of the profile (mix ratio, PHR (Hb), stutter, etc…) to find optimal genotypes, giving **WEIGHT** to the results.



Probable Genotypes
AC – 40%
BC – 25%
CC – 20%
CQ – 15%

Some Continuous Model Examples

- TrueAllele (Cybergenetics)
- STRmix (ESR [NZ] and Australian collaboration)
- DNA-View Mixture Solution (Charles Brenner)
- DNAmixtures (Graversen 2013a,b) – open source, but requires HUGIN.

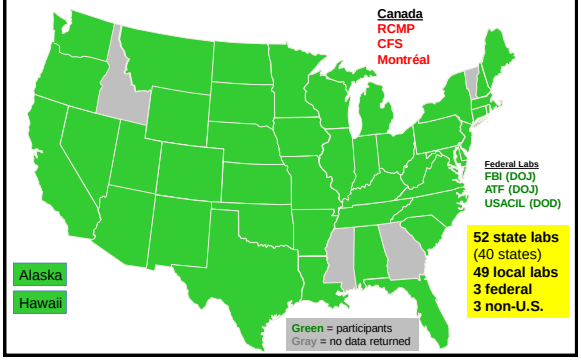
Weights may be determined by performing simulations of the data (Markov Chain Monte Carlo - MCMC).

Fully continuous methods

- Can model drop-out and provide weights for the LR calculation
- Speed of analysis – can vary
- Attempts to use all of the data

MIX13 Participants from **108 Laboratories**

46 states had at least one lab participate



Due to the number of laboratories responding and the federal, state, and local coverage obtained, this MIX13 interlaboratory study can be assumed to provide **a reasonable representation of current U.S. forensic DNA lab procedures across the community**

Purpose of MIX13 Cases

	Challenge provided to study responses
Case 1	~1:1 mixture (2-person)
Case 2	**Low template** profile with potential dropout (3-person)
Case 3	Potential **relative** involved (3-person)
Case 4	Minor component (2-person)
Case 5	Complex mixture (>3-person) with **# of contributors**; inclusion/exclusion issues

According to German Stain Commission (2009) mixture types: 1 = A, 2 = C, 3 = ?, 4 = B, 5 = ?

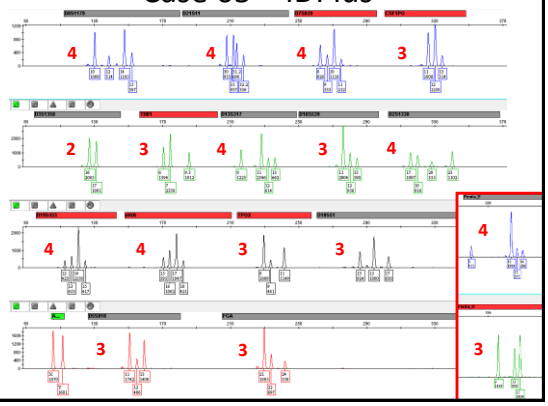
Case 05 – Ski Mask (Robbery Evidence)

Complex mixture (>3-person) with # of contributors; inclusion/exclusion issues

Scenario

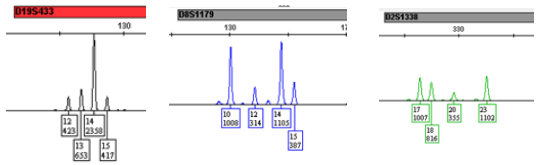
- Evidence: Ski mask recovered at a bank robbery.
- A number of gang-related robberies have targeted several banks in the city. The robberies have typically involved 2-3 perpetrators. A ski mask was recovered in a trash can one block away from the latest bank robbery and is submitted for DNA testing.
- A confidential informant has implicated two suspects in at least three of the armed robberies. Police have obtained buccal swab references from the two suspects identified from the CI, and another known accomplice of the suspects.

Case 05 – IDPlus



No more than 4 alleles at a locus

- Suggests a 2 person mixture



- Peak Height information does not agree

		#1	#2	#3	#4	#5	#6
GT36866_MT97199	UT58299_Y12	0	3	9	4	0	0
MT94803_MT97199	UT57301_TT50705	0	3	7	6	0	0
GT36866_OT07776	UT58299_TT50705	0	2	8	6	0	0
GT36885_MT97192	WT51386_TT50705	0	2	8	6	0	0
GT38069_GT38119	UT58299_MT94884	0	2	8	6	0	0
GT38098_MT97199	UT57301_TT50705	0	2	8	6	0	0
MT94803_MT97199	UT58299_Y12	0	3	6	7	0	0
MT97126_MT97173	UT58318_UT57299	0	3	6	7	0	0
MT97126_MT97173	UT58318_TT50705	0	3	6	7	0	0

Note: All samples are unrelated
(relative testing, mtDNA, Y-STRs, X-STRs, etc…)

Case 05 – 3 Suspects

Individual	
Suspect 5A	Included
Suspect 5B	Included
Suspect 5C	Not in the mixture

MIX13 Case 5 Outcomes with Suspect C

(whose genotypes were not present in the mixture)

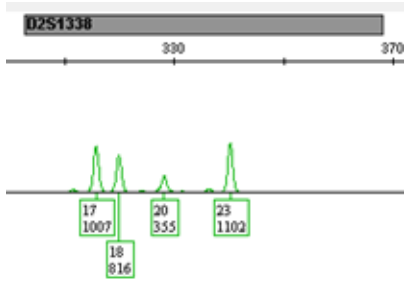
# Labs	Report Conclusions	Reasons given
7	Exclude Suspect C	detailed genotype checks (ID+); TrueAllele negative LR (ID+); assumed major/minor and suspects did not fit (ID+); 4 of 18 labs noted Penta E missing allele 15 (PP16HS)
3	Inconclusive with C only (A & B included)	All these labs used PP16HS
22	Inconclusive for A, B, and C	
76	**Include & provide CPI statistics**	*All over the road…*

Range of CPI stats for Caucasian population:
FBI allele frequencies: **1 in 9** (Labs 12 & 54) to **1 in 344,000** (Lab 107)

Case 05

"Couldn't help but note the need for mix deconvolution software tools for case 05"

(a) Deconvolution as 3p mixture



GENOTYPE PROBABILITY DISTRIBUTION

D2S1338

[23,23]	[18,20]	[17,17]	3.1435619345160034E-4
[17,20]	[18,23]	[17,17]	0.013779123510160775
[18,20]	[18,23]	[17,17]	0.0025562385293281887
[20,20]	[18,23]	[17,17]	3.5330685147076245E-4
[20,23]	[18,23]	[17,17]	0.09463609425559072
[18,18]	[20,23]	[17,17]	1.3307620480543583E-4
[18,20]	[23,23]	[17,17]	2.2360678716779012E-4
[23,23]	[17,20]	[17,18]	1.860003332375718E-5
[18,20]	[17,23]	[17,18]	0.011194437871043312
[20,23]	[17,23]	[17,18]	0.0022887419156283734
[17,20]	[18,23]	[17,18]	0.0025434216996429106
[20,23]	[18,23]	[17,18]	4.670327695074493E-5
[17,18]	[20,23]	[17,18]	5.917624047373503E-5
[17,23]	[20,23]	[17,18]	2.2663906150796565E-5
[18,23]	[20,23]	[17,18]	1.1378843915710276E-5
[17,20]	[23,23]	[17,18]	4.217987388864801E-4
[18,20]	[23,23]	[17,18]	3.3877069097404465E-4

[20,23]	[23,23]	[17,18]	5.689421957855138E-6
[23,23]	[17,20]	[18,18]	2.0319364135196922E-6
[17,20]	[17,23]	[18,18]	0.012963941881616883
[18,20]	[17,23]	[18,18]	0.004694742192596937
[20,20]	[17,23]	[18,18]	5.370564243733586E-5
[20,23]	[17,23]	[18,18]	0.07806365212748431
[17,17]	[20,23]	[18,18]	4.020108042748191E-5
[17,23]	[20,23]	[18,18]	2.1225920381228785E-5
[17,20]	[23,23]	[18,18]	7.19930701590131E-5
[18,23]	[17,18]	[17,20]	2.5571138250140126E-5
[23,23]	[17,18]	[17,20]	0.01846580047822405
[23,23]	[18,18]	[17,20]	1.8006082679805273E-5
[18,18]	[17,23]	[17,20]	0.012773252464348113
[18,23]	[17,23]	[17,20]	0.0017543426388726942
[17,17]	[18,23]	[17,20]	0.015332554528576684
[17,18]	[18,23]	[17,20]	0.0027471155099582077
[17,20]	[18,23]	[17,20]	3.0322743401755406E-5
[17,23]	[18,23]	[17,20]	0.07381384148832777
[18,23]	[18,23]	[17,20]	2.3154696946062092E-4
[17,18]	[23,23]	[17,20]	1.6071054002930366E-4
[18,18]	[23,23]	[17,20]	1.5758448400850412E-4
[18,23]	[17,17]	[18,20]	1.1128759434046313E-5

[23,23]	[17,18]	[18,20]	0.006032975514541006
[17,18]	[17,23]	[18,20]	0.00808063598984532
[18,18]	[17,23]	[18,20]	0.006747373096974322
[18,20]	[17,23]	[18,20]	2.341415959578845E-5
[17,23]	[17,23]	[18,20]	0.0024700844253949536
[18,23]	[17,23]	[18,20]	0.07586022028066357
[23,23]	[17,23]	[18,20]	5.9645148876854965E-5
[17,17]	[18,23]	[18,20]	0.0031901401692259164
[17,23]	[18,23]	[18,20]	2.420817782507153E-4
[17,17]	[23,23]	[18,20]	8.84705114446474E-4
[17,18]	[23,23]	[18,20]	4.2464344986540767E-4
[18,18]	[17,23]	[20,20]	3.0313365233693005E-4
[17,17]	[18,23]	[20,20]	2.3336008195268463E-4
[17,23]	[18,23]	[20,20]	1.5036329460045721E-5
[18,20]	[17,18]	[17,23]	1.0003379266558484E-5
[20,23]	[17,18]	[17,23]	0.013604189415236835
[18,23]	[17,20]	[17,23]	3.238594037548309E-5
[17,23]	[18,20]	[17,23]	8.277796343077145E-5
[18,20]	[17,23]	[17,23]	0.0015531184128138287
[17,20]	[18,23]	[17,23]	0.07913420127236732
[18,20]	[18,23]	[17,23]	3.572144214967619E-4
[20,23]	[18,23]	[17,23]	3.1072996846747295E-5
[18,20]	[17,17]	[18,23]	2.3320377915164468E-5
[20,23]	[17,17]	[18,23]	5.867607151040711E-5

[17,20]	[17,18]	[18,23]	5.501858596607167E-6
[20,23]	[17,18]	[18,23]	0.00291845464045823
[17,23]	[17,20]	[18,23]	6.170834585058266E-5
[18,23]	[17,20]	[18,23]	8.221527334702755E-5
[17,20]	[17,23]	[18,23]	0.0026107882068911402
[18,20]	[17,23]	[18,23]	0.07008842674666035
[20,20]	[17,23]	[18,23]	1.2254139601534142E-5
[20,23]	[17,23]	[18,23]	3.1291820768203256E-5
[17,20]	[18,23]	[18,23]	2.1735467512619107E-4
[17,17]	[20,23]	[18,23]	3.532443303503465E-6
[18,18]	[17,17]	[20,23]	1.0253463748222446E-5
[18,23]	[17,17]	[20,23]	4.68908403119929E-6
[17,18]	[17,18]	[20,23]	1.419229433442985E-5
[17,23]	[17,18]	[20,23]	0.017445580835275917
[18,23]	[17,18]	[20,23]	0.003605405451028926
[20,23]	[17,18]	[20,23]	5.6269008374391474E-6
[23,23]	[17,18]	[20,23]	0.07682076351417463
[17,18]	[17,23]	[20,23]	0.0022137165711291844
[18,18]	[17,23]	[20,23]	0.10066731917876008
[18,23]	[17,23]	[20,23]	8.346569575534735E-5
[17,17]	[18,23]	[20,23]	0.07069522548085776
[17,18]	[18,23]	[20,23]	1.3617100026602736E-4
[17,23]	[18,23]	[20,23]	2.654021561658798E-5
[17,20]	[17,18]	[23,23]	0.020532436113574616

[18,20]	[17,18]	[23,23]	0.006249798760143661
[20,20]	[17,18]	[23,23]	1.1363213635606278E-4
[20,23]	[17,18]	[23,23]	0.07546711873604803
[18,18]	[17,20]	[23,23]	1.5942885706077583E-5
[18,23]	[17,20]	[23,23]	4.0638728270393845E-6
[17,17]	[18,20]	[23,23]	2.166356822414071 6E-5

93 !! Possible **Genotype** Combinations

```
Number of known contributors under Hp: 3
, Suspect_05A_ref.csv, Suspect_05B_ref.csv, Suspect_05C_ref.csv
Number of known contributors under Hd: 0


Locus 1(D8S1179): Pr(E|Hp) = 0.0, Pr(E|Hd) = 8.0E-5, LR = 0.0
Locus 2(D21S11): Pr(E|Hp) = 0.01875, Pr(E|Hd) = 3.0E-5, LR = 603.86846
Locus 3(D7S820): Pr(E|Hp) = 0.0, Pr(E|Hd) = 4.6E-4, LR = 0.0
Locus 4(CSF1PO): Pr(E|Hp) = 3.4E-4, Pr(E|Hd) = 0.00108, LR = 0.31407
Locus 5(D3S1358): Pr(E|Hp) = 0.19148, Pr(E|Hd) = 8.6E-4, LR = 222.85716
Locus 6(TH01): Pr(E|Hp) = 0.0, Pr(E|Hd) = 9.8E-4, LR = 0.0
Locus 7(D13S317): Pr(E|Hp) = 0.0, Pr(E|Hd) = 4.5E-4, LR = 0.0
Locus 8(D16S539): Pr(E|Hp) = 0.19217, Pr(E|Hd) = 0.00211, LR = 91.11187
Locus 9(D2S1338): Pr(E|Hp) = 0.0, Pr(E|Hd) = 5.0E-5, LR = 0.0
Locus 10(D19S433): Pr(E|Hp) = 0.0, Pr(E|Hd) = 5.3E-4, LR = 0.0
Locus 11(vWA): Pr(E|Hp) = 0.0, Pr(E|Hd) = 4.7E-4, LR = 0.0
Locus 12(TPOX): Pr(E|Hp) = 3.3E-4, Pr(E|Hd) = 0.00526, LR = 0.06341
Locus 13(D18S51): Pr(E|Hp) = 0.01176, Pr(E|Hd) = 7.0E-5, LR = 176.38643
Locus 14(D5S818): Pr(E|Hp) = 4.9E-4, Pr(E|Hd) = 0.00243, LR = 0.19993
Locus 15(FGA): Pr(E|Hp) = 0.0, Pr(E|Hd) = 1.8E-4, LR = 0.0
LR total = 0.0
```

LR Total = 0.0

Summary

- Probabilistic Methods make better use of the data than RMNE or the binary LR with 2p.
- The goal of the software programs should not be to simply “get bigger numbers” but to understand the details of these approaches and not treat the software as a “black box.”

Summary of Issues

- **Use of CPI has significant limitations when it comes to complex mixtures** because this approach delivers information regarding the presence of alleles rather than specific suspect genotypes
- A CPI approach **has the potential to falsely include innocent suspects** as demonstrated in MIX13 Case 5
- The U.S. forensic DNA community adopted CPI for simplicity in 1990s and early 2000s when 2-person mixtures were common and have now inappropriately extrapolated the approach to more complex mixtures

Acknowledgments

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