NIJ CONFERENCE, 2012

Statistical Analysis

It doesn't have to be a Shakespearean tragedy!

NIJ
National
Institute
of Justice

BOSTON
UNIVERSITY

NIST

In every workshop presented and supported by our NIJ grant

- Participants said they needed more training in
  - Mixture analysis
  - **Statistics** related to mixtures

Statistics

A Tragedy in 400 Quadrillion Acts

http://es.wikipedia.org/wiki/William_Shakespeare

“Though this be madness,
yet there is method in't.”

— William Shakespeare, *Hamlet*

Stats Required for Inclusions

SWGDAM Interpretation Guideline 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.

DAB Recommendations on Statistics

February 23, 2000

Forensic Sci. Comm. 2(3); available on-line at http://www.fbi.gov/hq/lab/fsc/backissu/july2000/dnastat.htm

“The DAB finds either one or both PE or LR calculations acceptable and strongly recommends that one or both calculations be carried out whenever feasible and a mixture is indicated”

- Probability of exclusion (PE)
  - Devlin, B. (1993) Forensic inference from genetic markers. *Statistical Methods in Medical Research* 2: 241–262.
- Likelihood ratios (LR)
  - Evett, I. W. and Weir, B. S. (1998) *Interpreting DNA Evidence*. Sinauer, Sunderland, Massachusetts.

Statistical Approaches with Mixtures

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

“Exclusionary” Approach

Random Man Not Excluded (RMNE)

Combined Prob. of Inclusion (CPI)

Combined Prob. of Exclusion (CPE)

“Allele-centric”

“Inferred Genotype” Approach

Random Match Probability [modified] (mRMP)

Likelihood Ratio (LR)

“Genotype-centric”

Forensic Science International: Genetics 2 (2008) 343–348

A discussion of the merits of random man not excluded and likelihood ratios

John Buckleton [a,*], James Curran [b]

[a] *ESR, PB 92021, Auckland, New Zealand*

[b] *Department of Statistics, University of Auckland, PB 92019, Auckland, New Zealand*

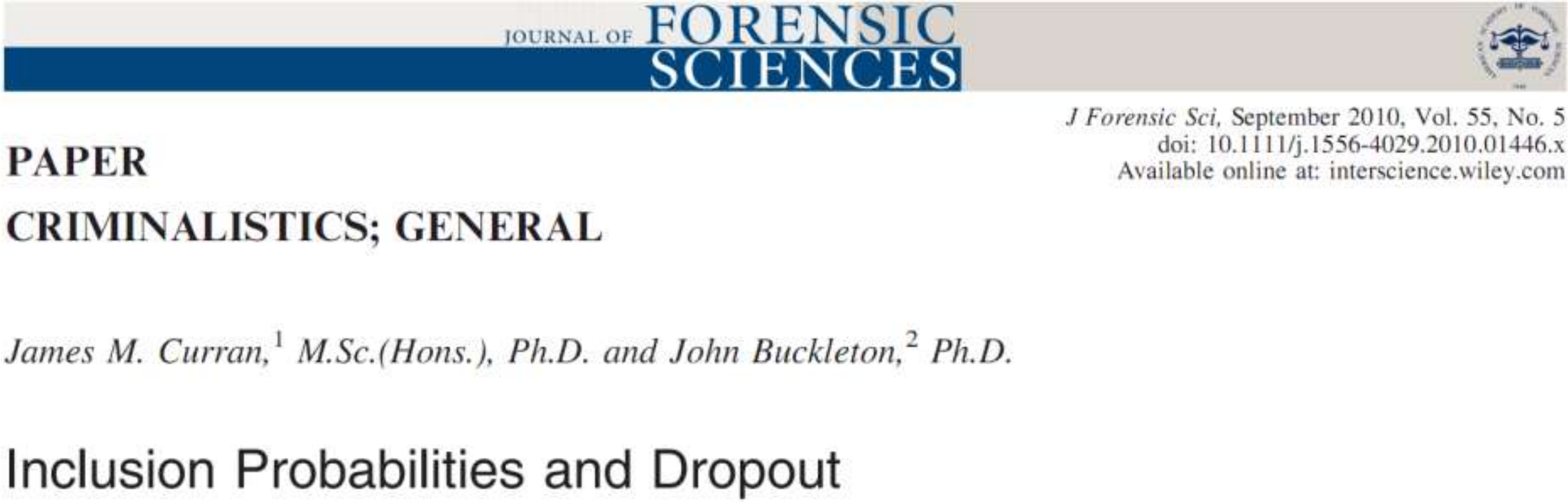
Received 15 January 2008; received in revised form 29 April 2008; accepted 1 May 2008

We conclude that the two matters that appear to have real force are:

(1) LRs are more difficult to present in court and

(2) the RMNE statistic wastes information that should be utilised.

Curran and Buckleton (2010)



JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, September 2010, Vol. 55, No. 5
doi: 10.1111/j.1556-4029.2010.01446.x
Available online at: interscience.wiley.com

PAPER

CRIMINALISTICS; GENERAL

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

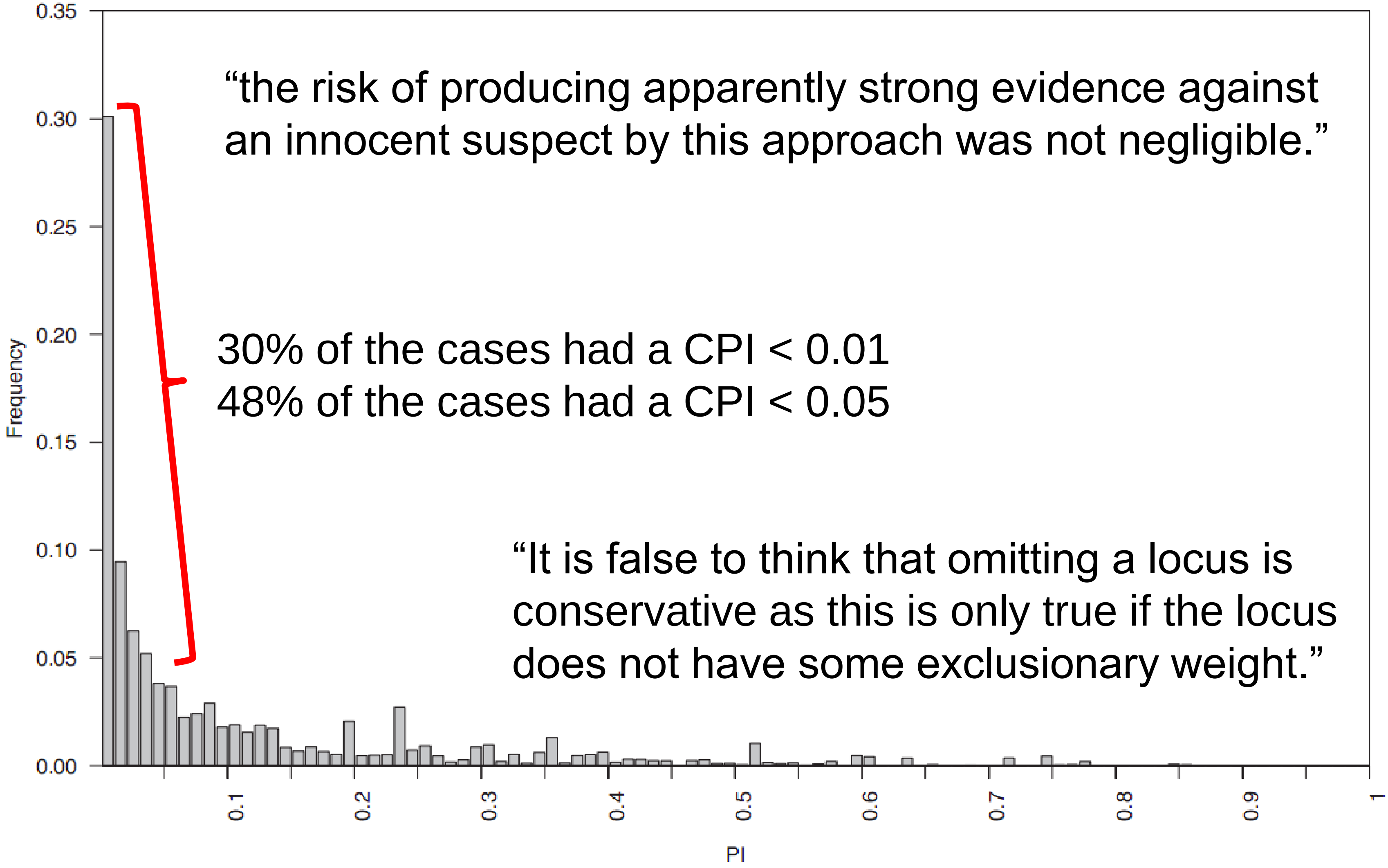
Inclusion Probabilities and Dropout

Created 1000 Two-person Mixtures (Budowle *et al.*1999 AfAm freq.).

Created 10,000 “third person” genotypes.

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

Curran and Buckleton (2010)

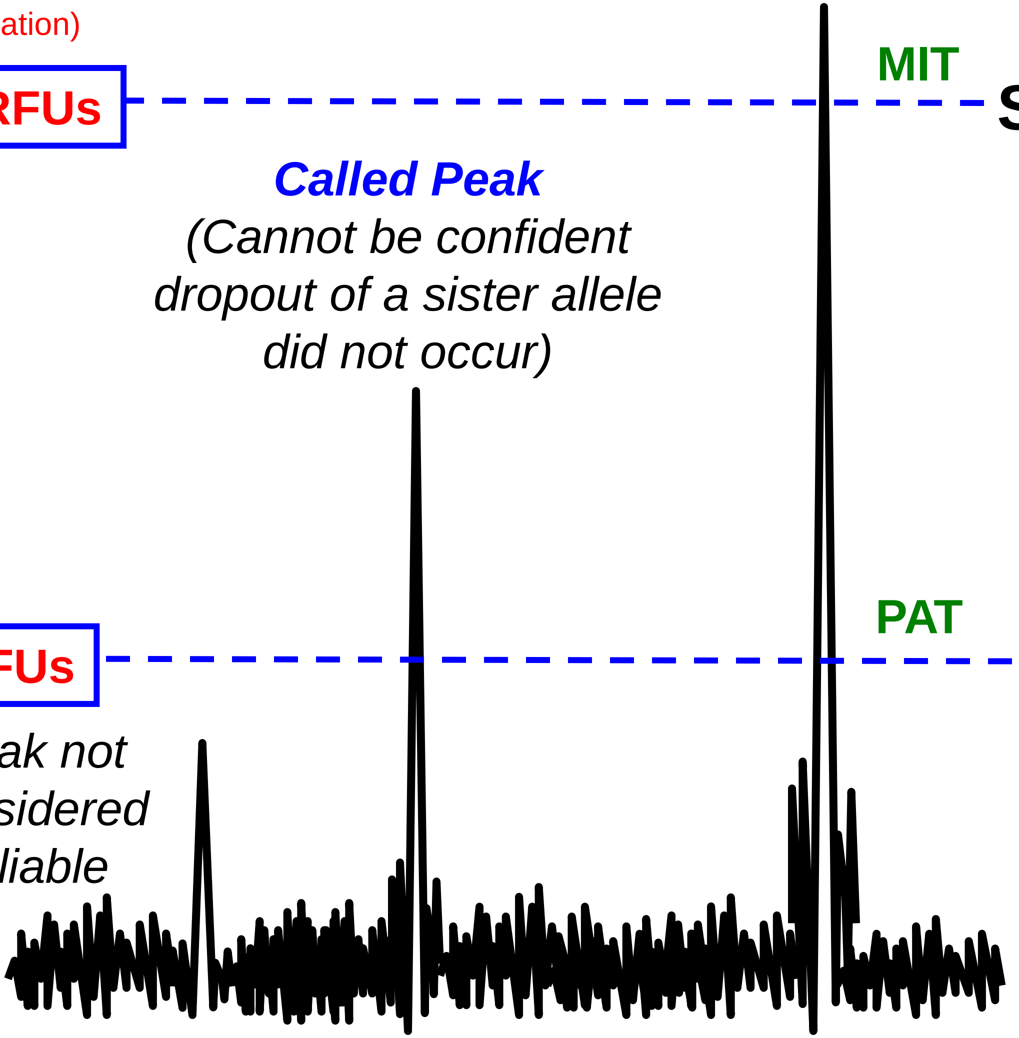


“the risk of producing apparently strong evidence against an innocent suspect by this approach was not negligible.”

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.”

Review of Two Thresholds



Example values
(empirically determined based on own internal validation)

Called Peak
(Greater confidence a sister allele has not dropped out)

MIT

200 RFUs

Stochastic Threshold

The value above which it is reasonable to assume that allelic dropout of a sister allele has not occurred

Called Peak
(Cannot be confident dropout of a sister allele did not occur)

PAT

50 RFUs

Analytical Threshold

Minimum threshold for data comparison and peak detection in the DNA typing process

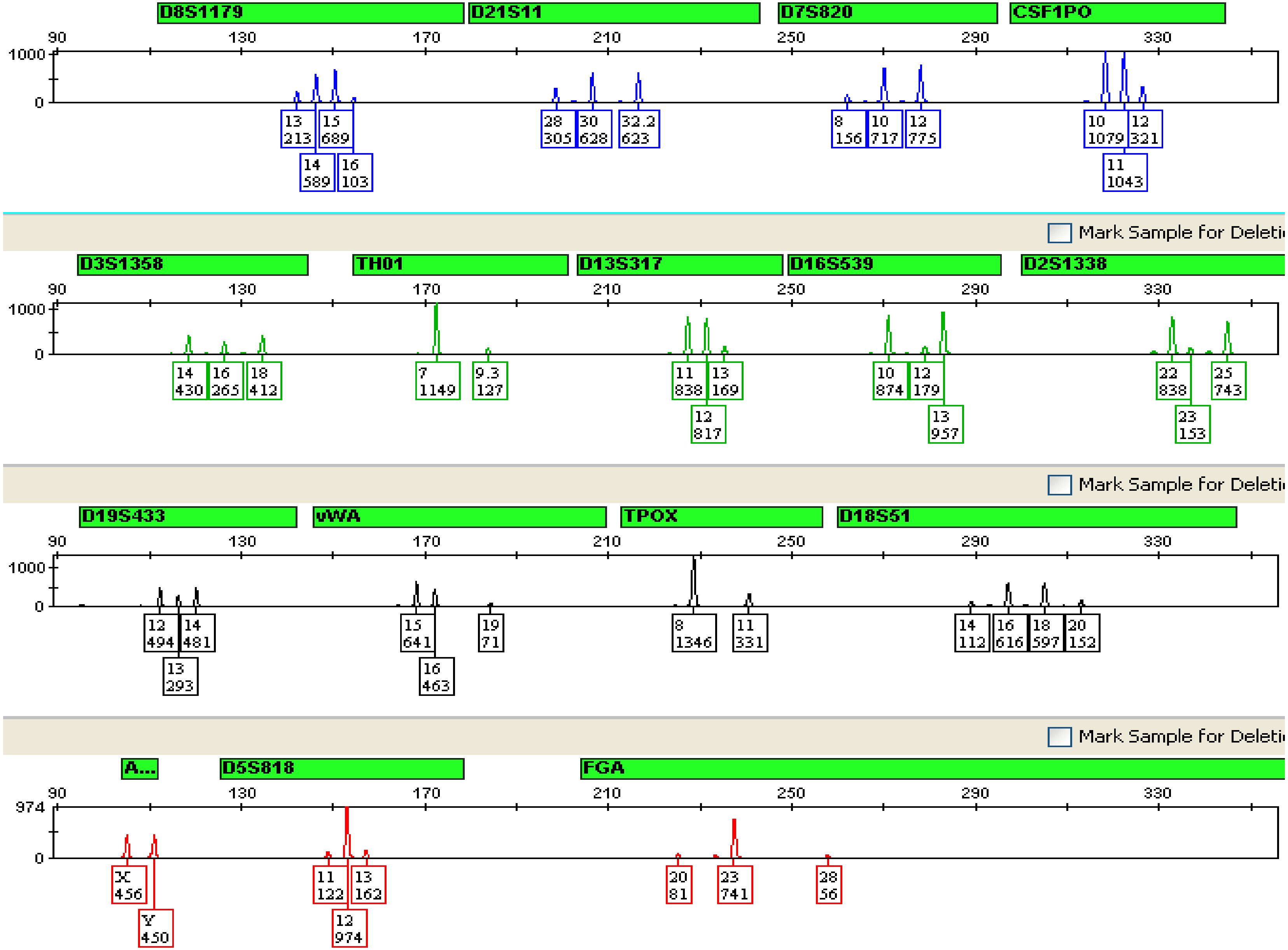
Peak not considered reliable

Noise

Butler, J.M. (2010) *Fundamentals of Forensic DNA Typing*. Elsevier Academic Press: San Diego.

2-person Mixture

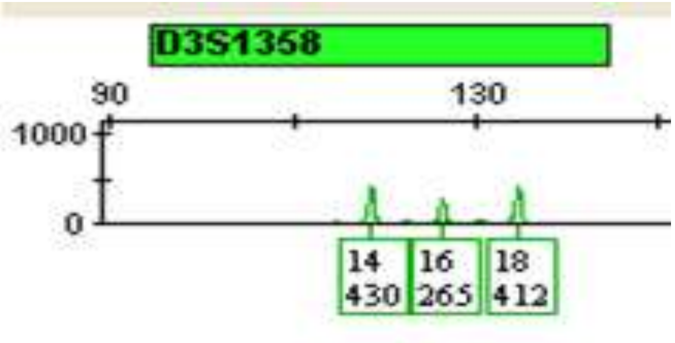
2-Person Mixture

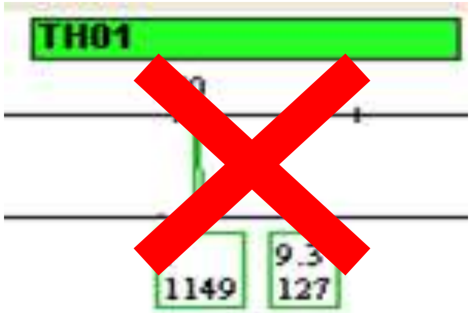


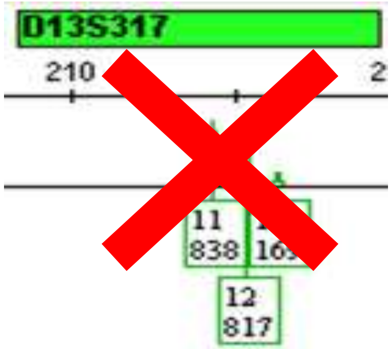
If CPI/CPE Stats are Used

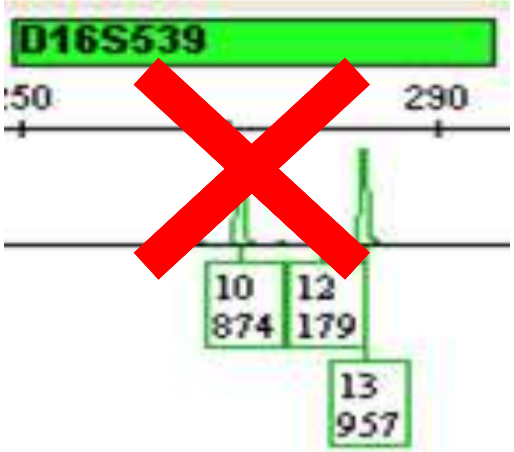
Since exclusionary statistics cannot adjust for the possibility of dropout, and does not take the number of contributors into account, any loci with alleles below the stochastic threshold cannot be used in the CPI statistic.

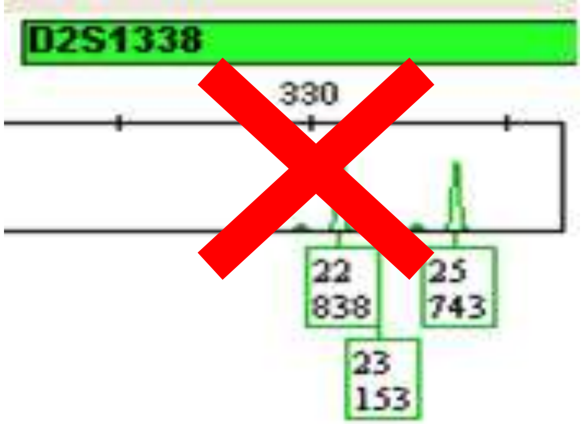
If CPI/CPE Stats are Used
(ST = 200 RFU)









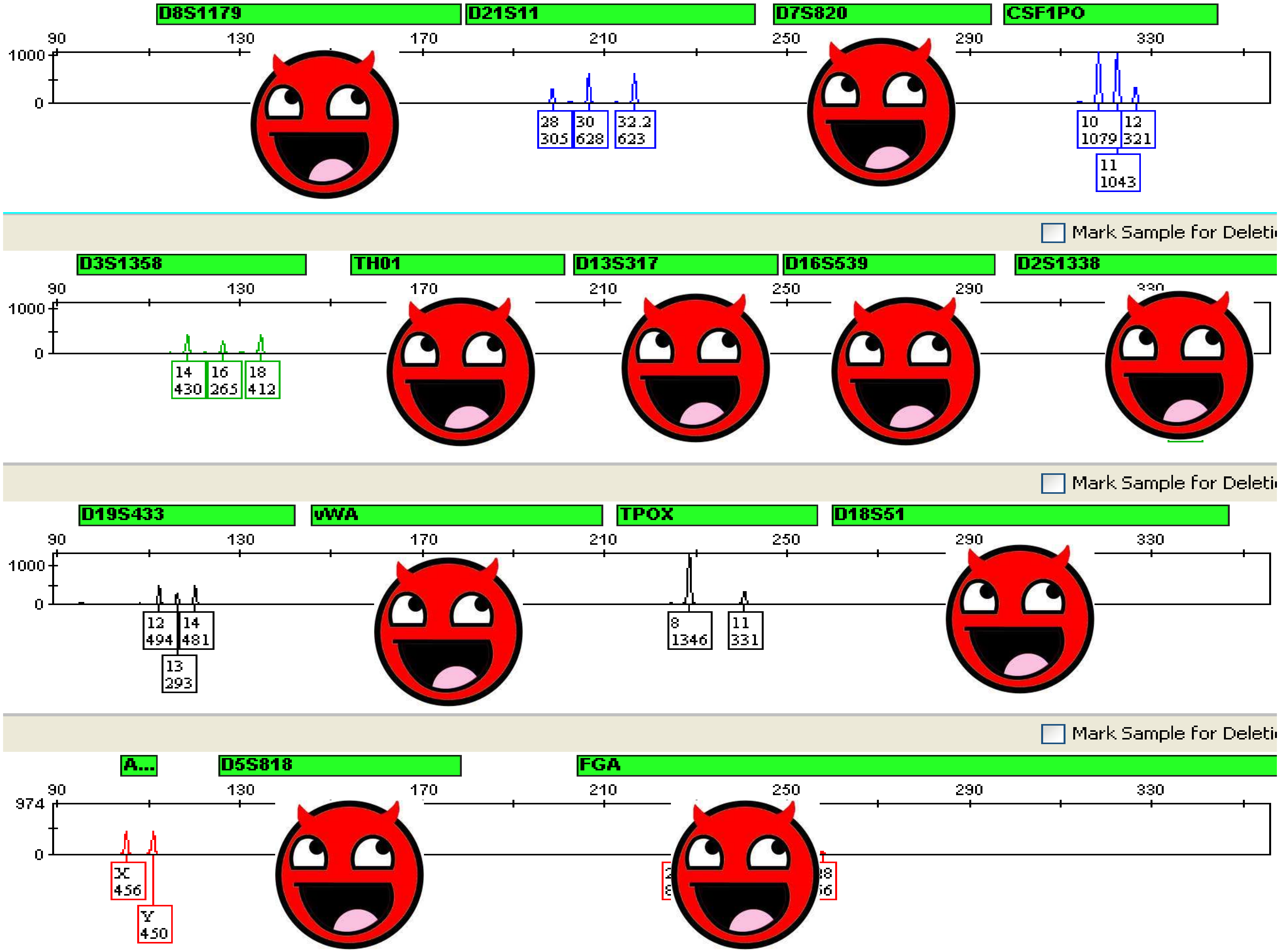


Shakespeare on Allelic Drop-Out

“Hell is empty and all the devils are here.”
— William Shakespeare, *The Tempest*

http://es.wikipedia.org/wiki/William_Shakespeare

If CPI/CPE Stats are Used



If CPI/CPE Stats are Used

Can use

- D21
- CSF
- D3
- D19
- TPOX

Cannot use

- D8
- D7
- TH01
- D13
- D16
- D2
- vWA
- D18
- D5
- FGA

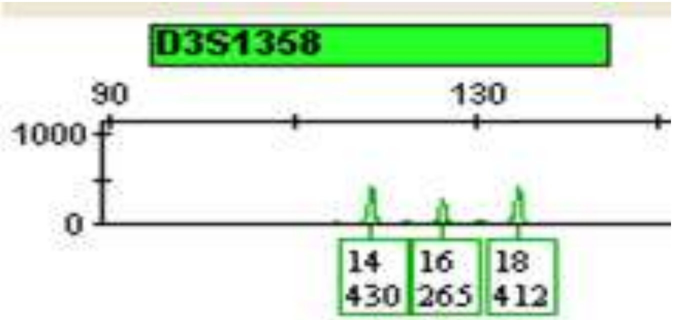
Impact: discarding 2/3 of the data

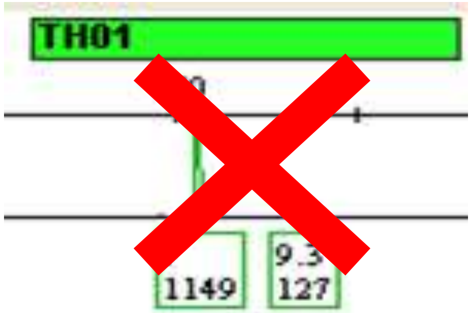
If CPI/CPE Stats are Used

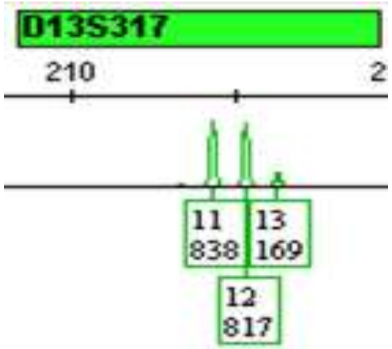
- CPI statistics using FBI Caucasian Frequencies

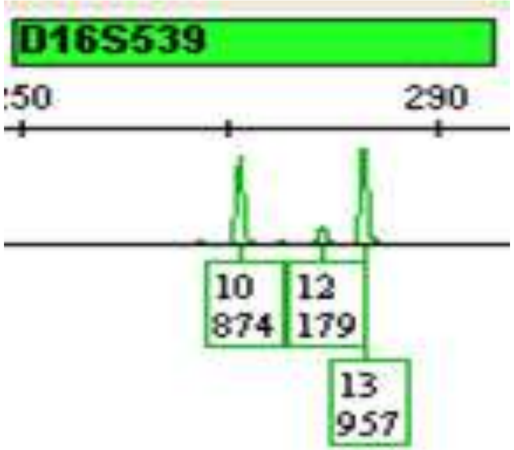
- 1 in 71 Caucasians included
- 98.59% Caucasians excluded

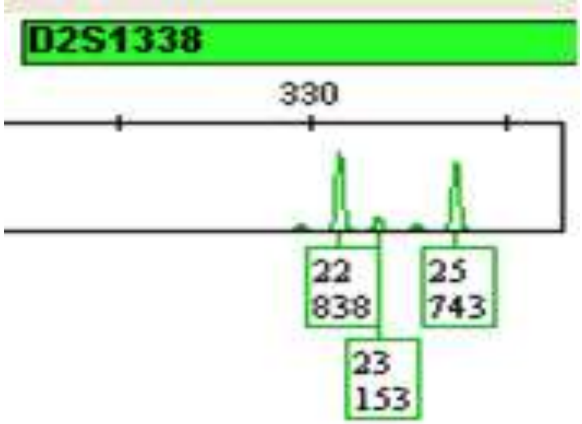
If CPI/CPE Stats are Used
(ST = 150 RFU)









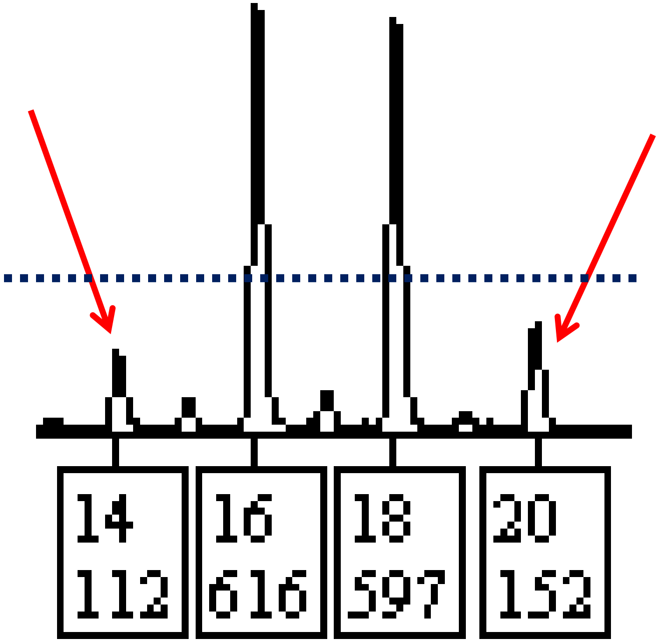


The impact of changing thresholds

If mRMP/LR Stats are Used

- Since there is an assumption to the number of contributors, it is possible to use data that falls below the ST.

mRMP - D18S51



If Assume 2 Contributors….

Major	Minor
16,18	14,20

$$\mathrm{mRMP}_{\mathrm{minor}} = 2pq$$

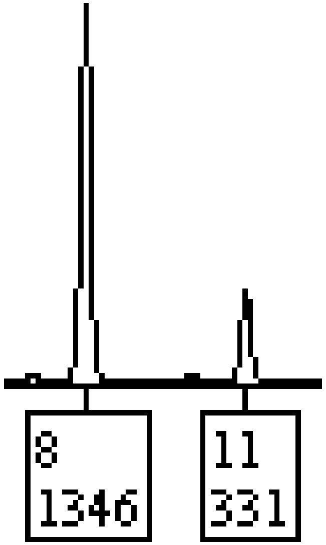
$$= 2 \times f(14) \times f(20)$$

$$= 2 \times (0.1735) \times (0.0255)$$

$$= 0.00884 \quad \text{or 1 in 113}$$

(LR = 113)

mRMP - TPOX



If Assume 2 Contributors….

Major	Minor
8,8	11,8 *OR* 11,11

mRMP = 8,11 + 11,11

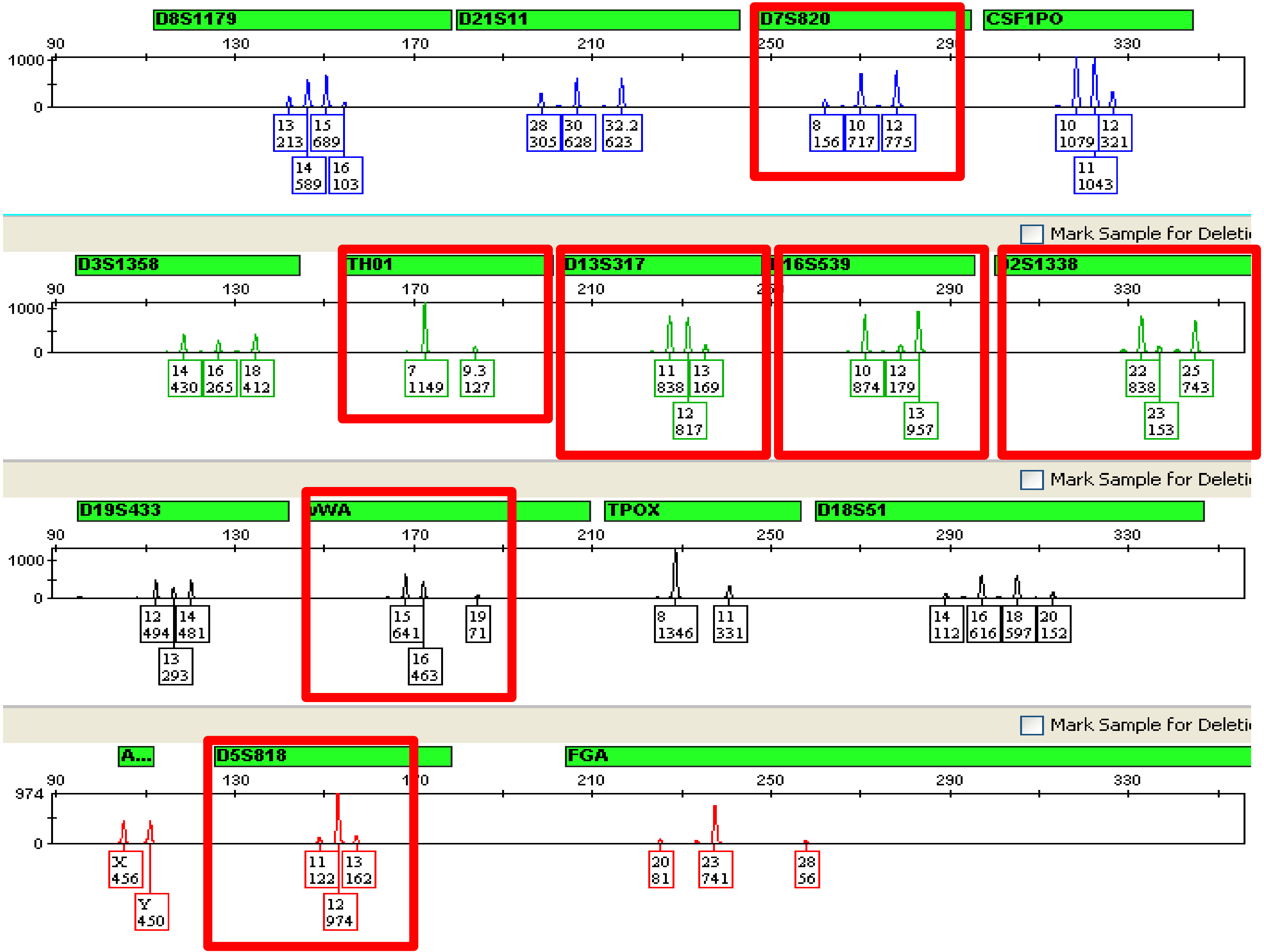
$$\text{mRMP} = 2pq + (q^2 + q(1-q)\theta)$$

$$\text{mRMP} = 2(0.5443)(0.2537) + (0.2537)^2 + (0.2537)(0.7463)(0.01)$$

= 0.3424 or 1 in 2.9

mRMP/LR

Potential for Drop-out



If mRMP/LR Stats are Used

Can use

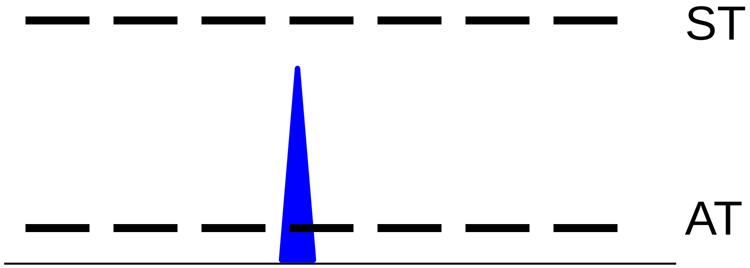
D8
D21
D18
D3
D19
TPOX
FGA
CSF

Loci with potential D-out

D7
TH01
D13
D16
D2
vWA
D5

The “2p” Rule

- The “2p” rule can be used to statistically account for zygosity ambiguity – i.e. is this single peak below the stochastic threshold the result of a homozygous genotype or the result of a heterozygous genotype with allele drop-out of the sister allele?



“2p” or not “2p”… That is the question.

Shakespeare on “2p”

http://es.wikipedia.org/wiki/William_Shakespeare

“Drink sir, is a great provoker of three things…. nose painting, sleep and urine.”

— William Shakespeare, *Macbeth*

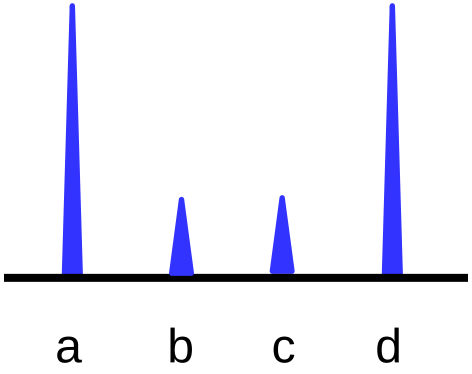
2p – SWGDAM Guidelines

- 5.2.1.3.1. The formula 2p, as described in recommendation 4.1 of NRCII, may be applied to this result.

- 5.2.1.3.2. Instead of using 2p, the algebraically identical formulae **$2p - p^2$** and **$p^2 + 2p(1-p)$** may be used to address this situation without double-counting the proportion of homozygotes in the population.

The Likelihood Ratio

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

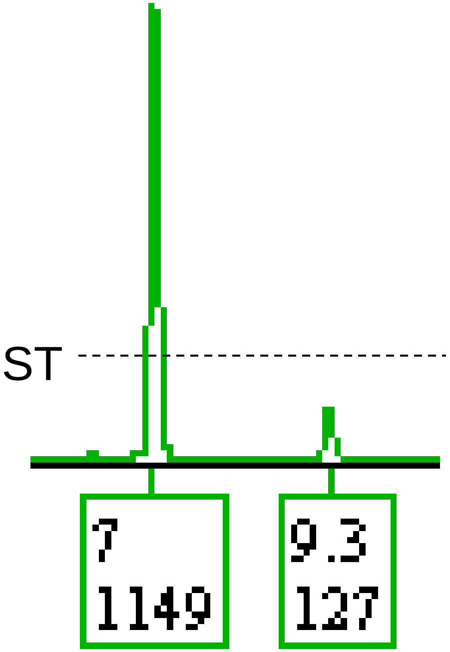


$$\frac{P(E|H_1)}{P(E|H_2)}$$

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

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

Macbeth/Duncan Profile - TH01



Major – 7, 7

Possible Minor Contributors

7, 9.3	(2pq)
9.3, 9.3	p^2
9.3, ?	2p (or $p^2 + 2p(1 - p)$)

Macbeth/Duncan Profile - TH01

$$\frac{P(E|H_1)}{P(E|H_2)} = \frac{V \,\&\, S}{V \,\&\, U} = \frac{\cancel{f_7^2 + f_7\,(1\text{-}f_7)\theta} \;\&\; 1}{\cancel{f_7^2 + f_7\,(1\text{-}f_7)\theta} \;\&\; 2p}$$

$p^2 + 2p(1 - p)$

V = 7, 7

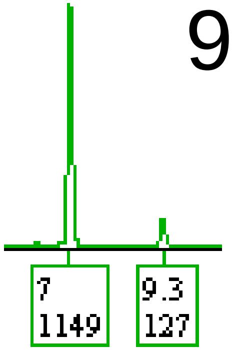
U = 7, 9.3

9.3, 9.3

9.3, ?

$$= \frac{1}{f_{9.3}^2 + 2f_{9.3}\,(1\text{-}f_{9.3})}$$

$$= \; 1 \,/\, 0.5175 \; = \boxed{1.93}$$



$f_{9.3} = 0.3054$

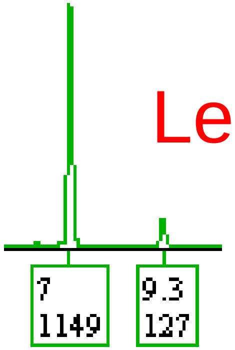
Macbeth/Duncan Profile - TH01

$$\frac{P(E|H_1)}{P(E|H_2)} = \frac{V \,\&\, S}{V \,\&\, U} = \frac{1}{p^2 + p(1-p)\theta + 2pq}$$

V = 7, 7

U = 7, 9.3
9.3, 9.3

$$= \frac{1}{f_{9.3}^{2} + f_{9.3}(1-f_{9.3})\theta + 2f_{9.3}f_7}$$



Let ST = 125 RFU

$f_{9.3} = 0.3054$

$f_7 = 0.1724$

$$= 1 / 0.2007 = \boxed{4.98}$$

Macbeth/Duncan Profile - TH01

	LR
ST = 200 (2p is used)	1.93
ST = 125 (2pq is used)	4.98

2p is conservative…

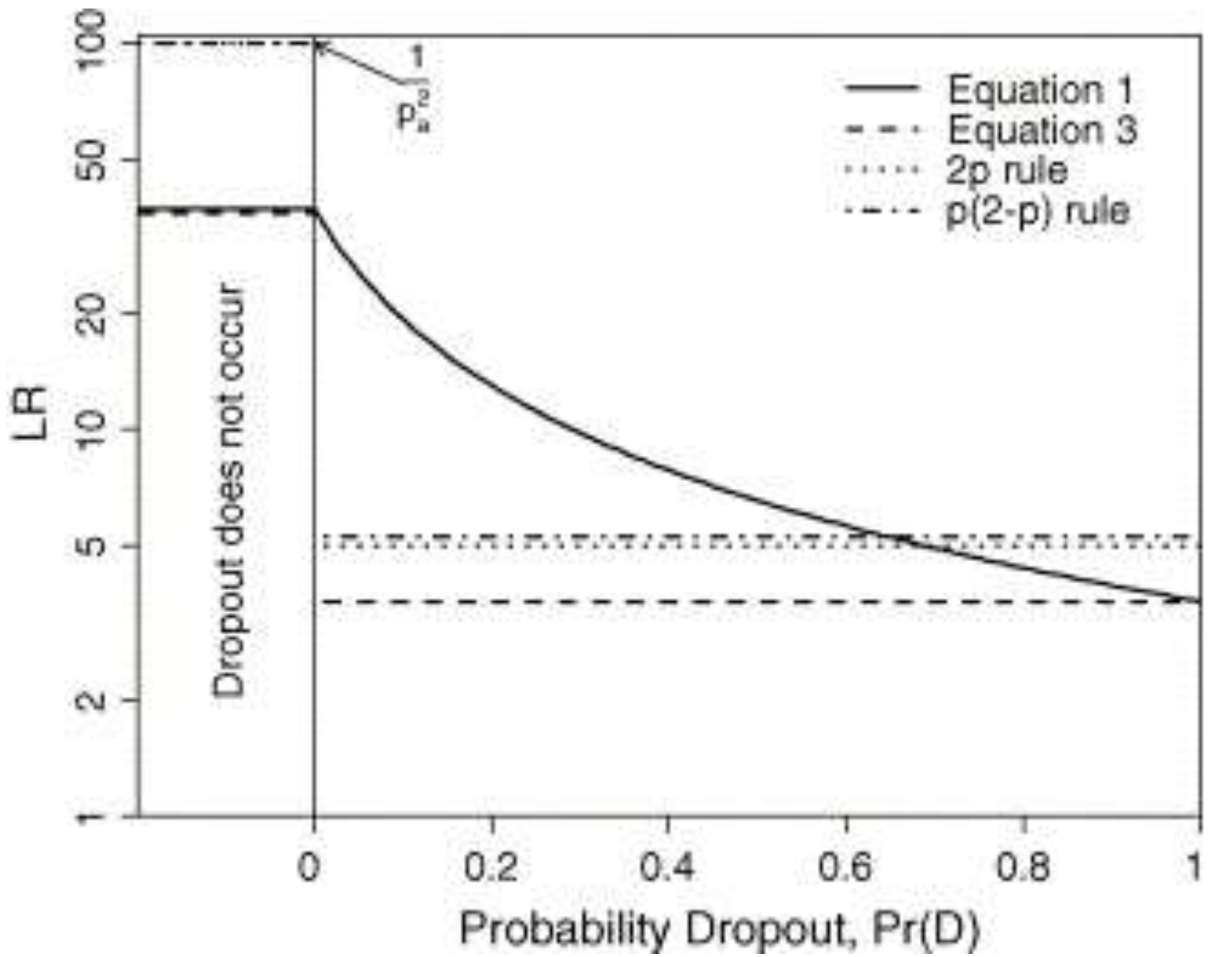
The “2p” Rule

- “This rule arose during the VNTR era. At that time many smaller alleles “ran off the end of the gel” and were not visualised.”

- Buckleton and Triggs (2006)

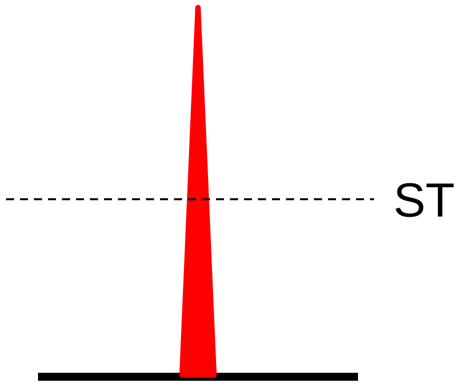
Is the 2*p* rule always conservative?”

The “2p” Rule



Stain = aa

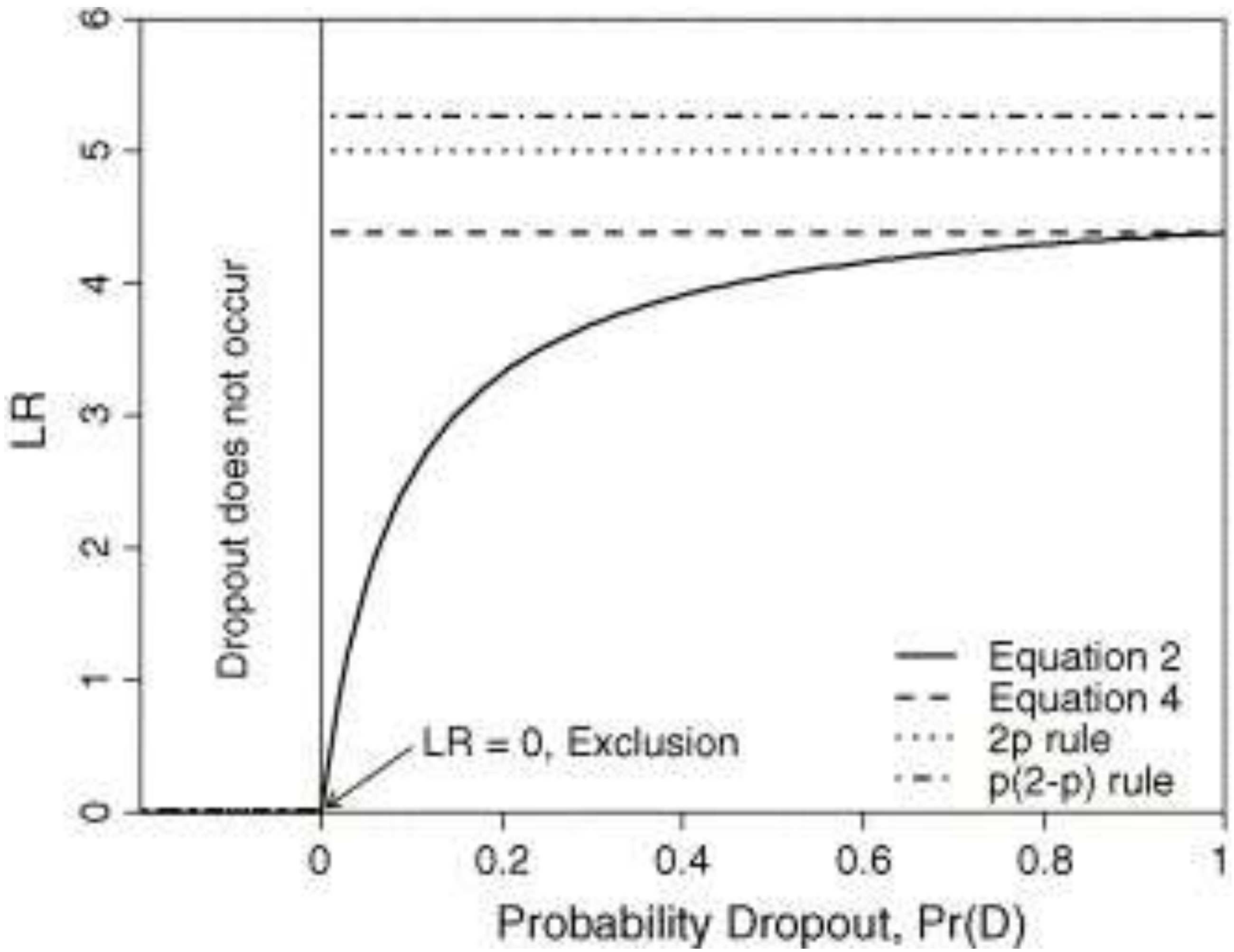
Suspect = aa



LR = 100

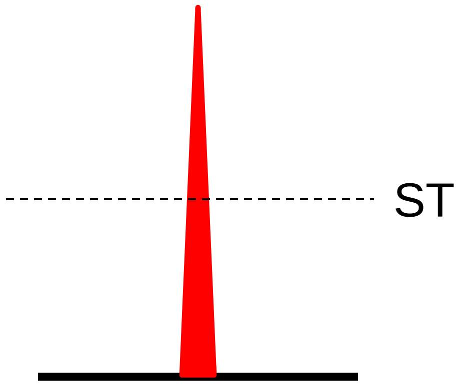
f(a) = 0.10 $1/p^2 = 100$ $1/2p = 5$

The “2p” Rule



Stain = aa

Suspect = ab



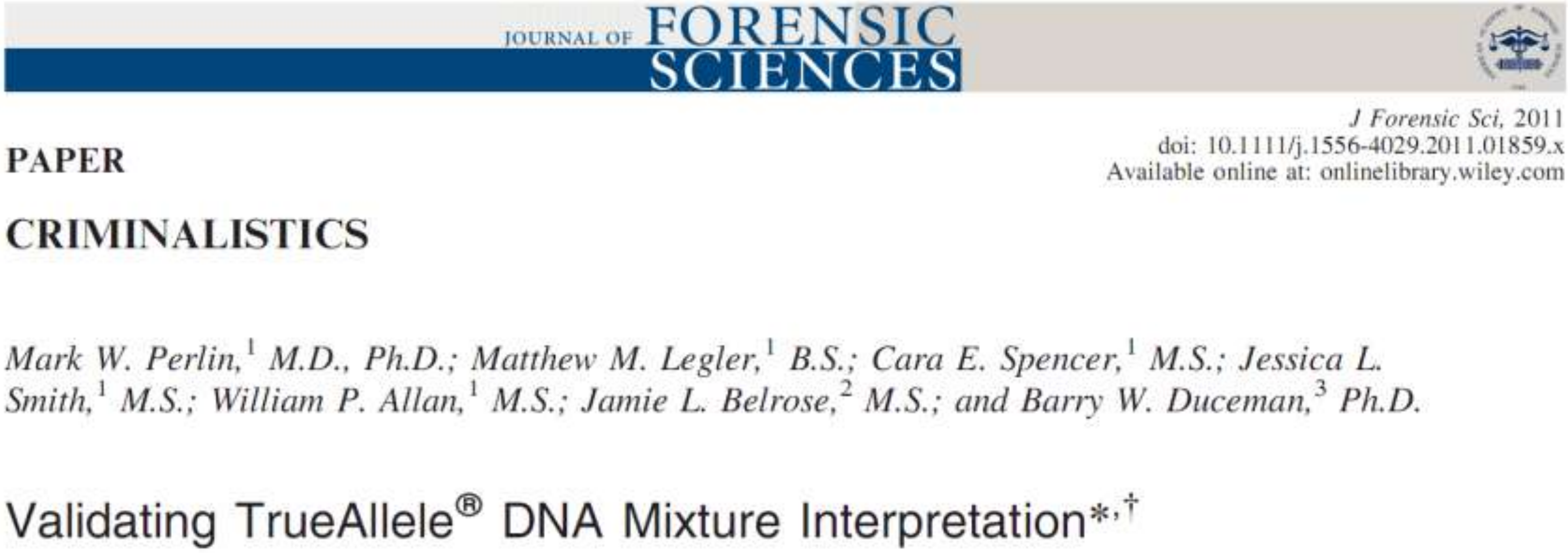
Exclusion

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

Is there a way forward?

Gill and Buckleton *JFS*
55: 265-268 (2010)

- “The purpose of the ISFG DNA commission document was to provide a way forward to demonstrate the use of ***probabilistic models to circumvent the requirement for a threshold*** and to safeguard the legitimate interests of defendants.”



JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, 2011
doi: 10.1111/j.1556-4029.2011.01859.x
Available online at: onlinelibrary.wiley.com

PAPER

CRIMINALISTICS

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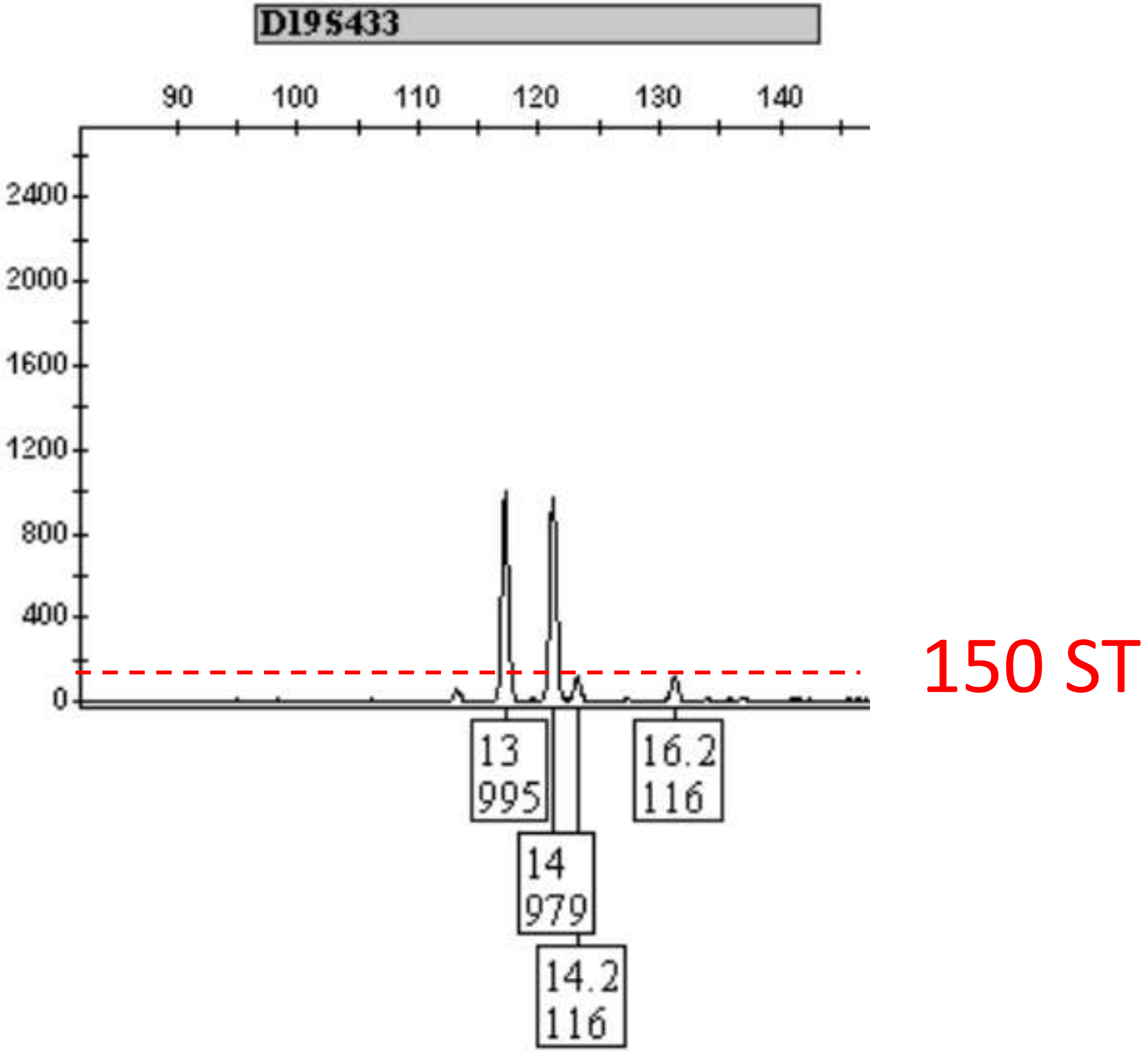
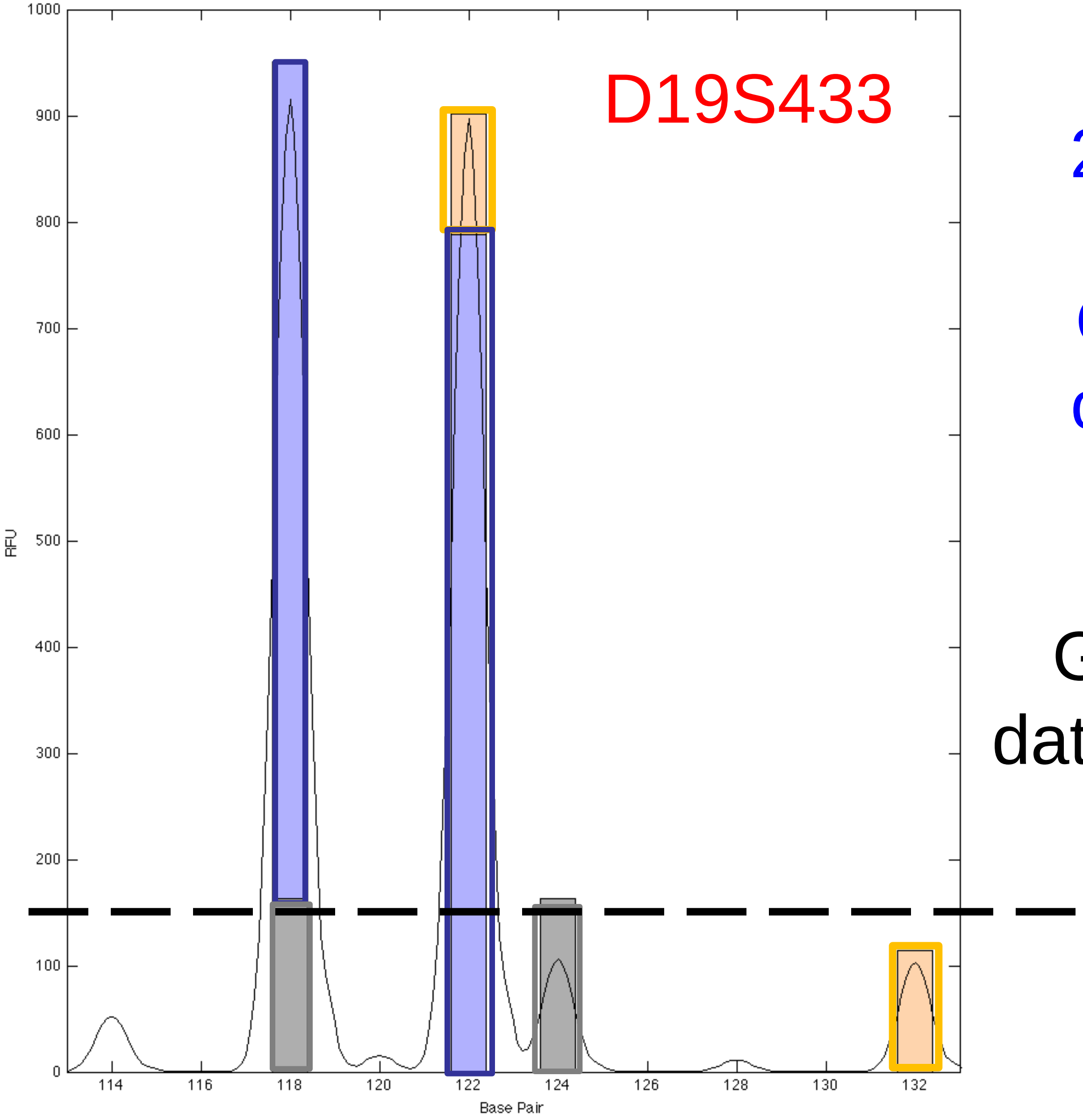
Validating TrueAllele® DNA Mixture Interpretation*,†

- Quantitative computer interpretation using
  Markov Chain Monte Carlo testing
- Models peak uncertainty and infers possible genotypes
- Results are presented as the Combined LR

3 Person Mixture



Review of One Replicate (of 50K)



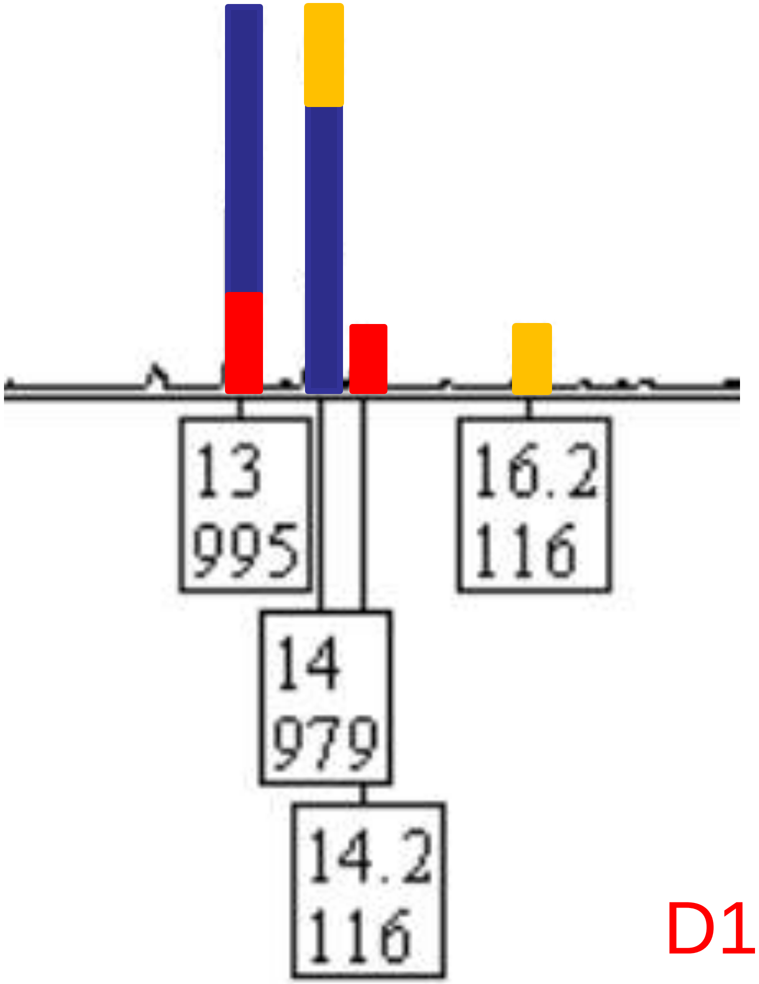
150 RFU

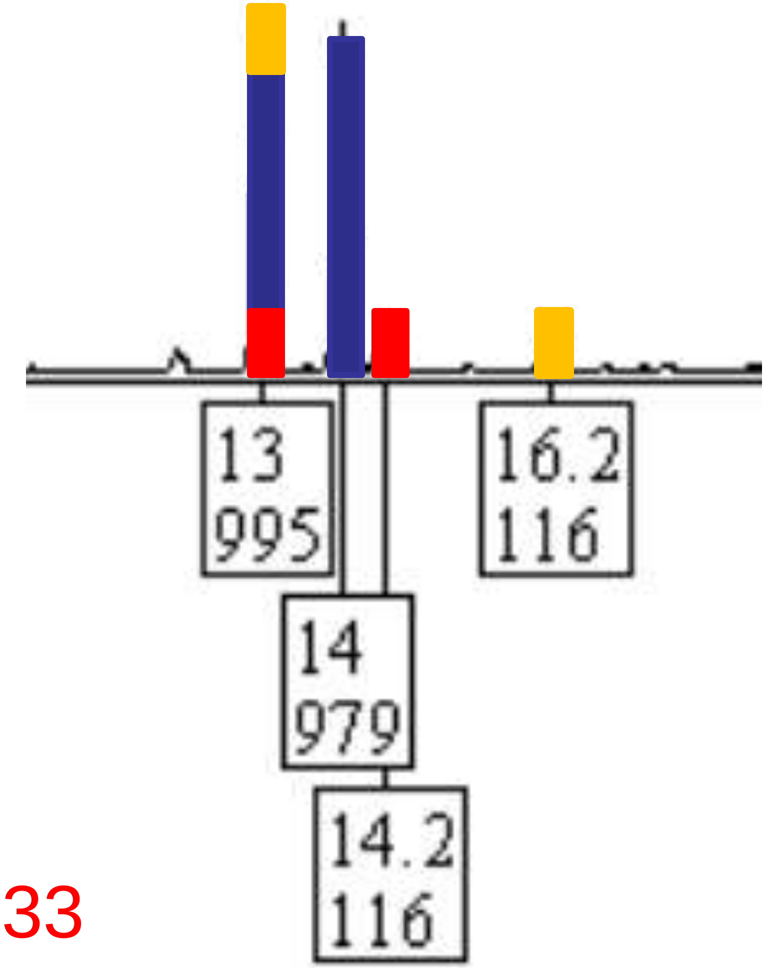
3P mixture,
2 Unknowns,

Conditioned
on the Victim
(major)

Good fit of the
data to the model

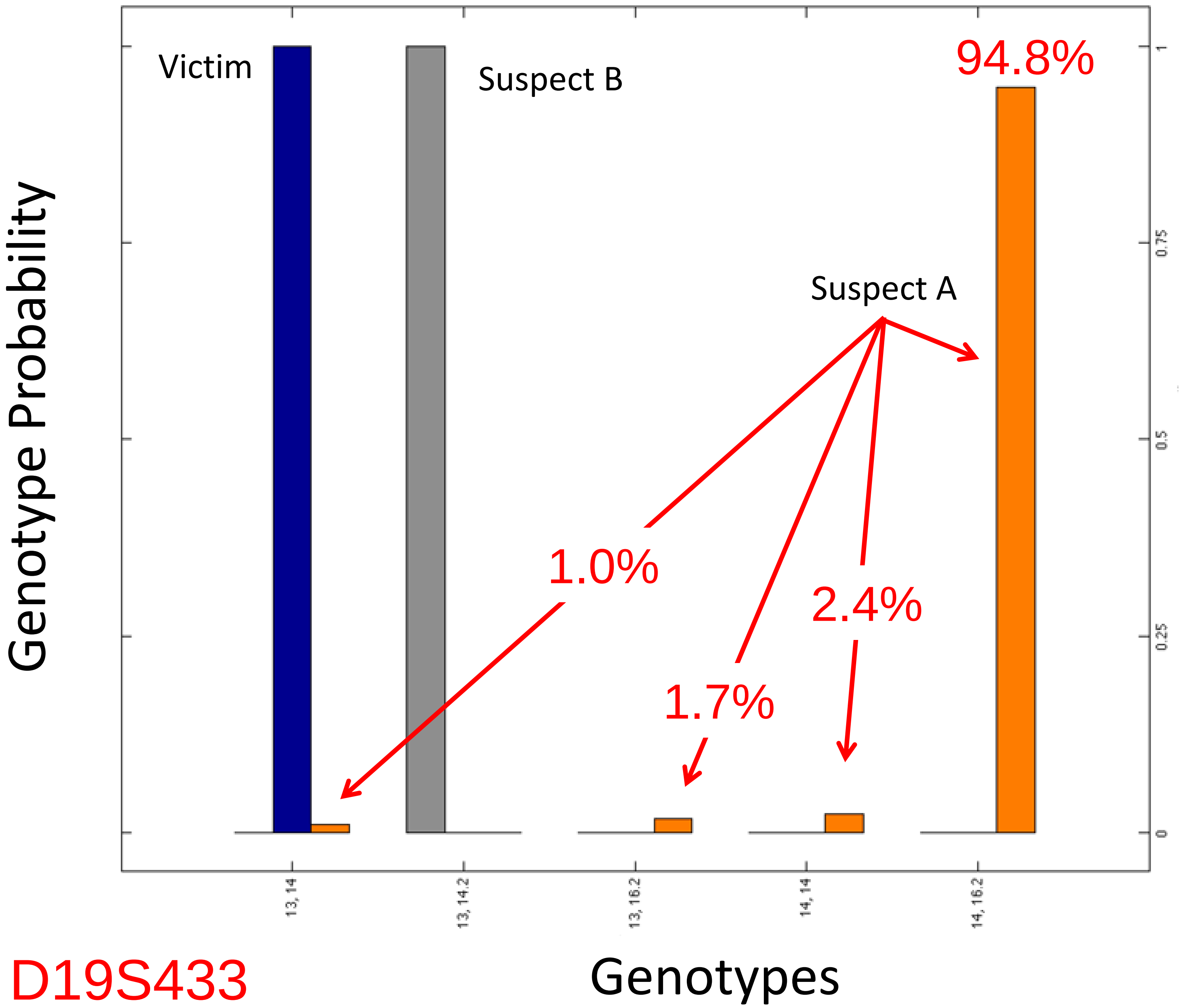
Alternative Explanations of the Data





D19S433

D19S433



14,16.2	**(94.8)**
14,14	**(2.4)**
13,16.2	**(1.7)**
13,14	**(1.0)**

Determining the LR for D19S433

Suspect A = 14, 16.2

$H_P = 0.967$

Allele Pair	Probability Before Conditioning
14, 16.2	0.967
14, 14	0.003
13, 16.2	0.026
13, 14	0.001

$$LR = \frac{0.967}{\quad}$$

Determining the LR for D19S433

Suspect A = 14, 16.2

$H_P = 0.967$

Allele Pair	Probability Before Conditioning	Genotype Frequency	Probability * Genotype Freq
14, 16.2	0.967	0.0120	0.01164
14, 14	0.003	0.0498	0.00013
13, 16.2	0.026	0.0131	0.00034
13, 14	0.001	0.1082	0.00009
		sum	**0.0122**

$$LR = \frac{0.967}{0.0122} = 79.26$$

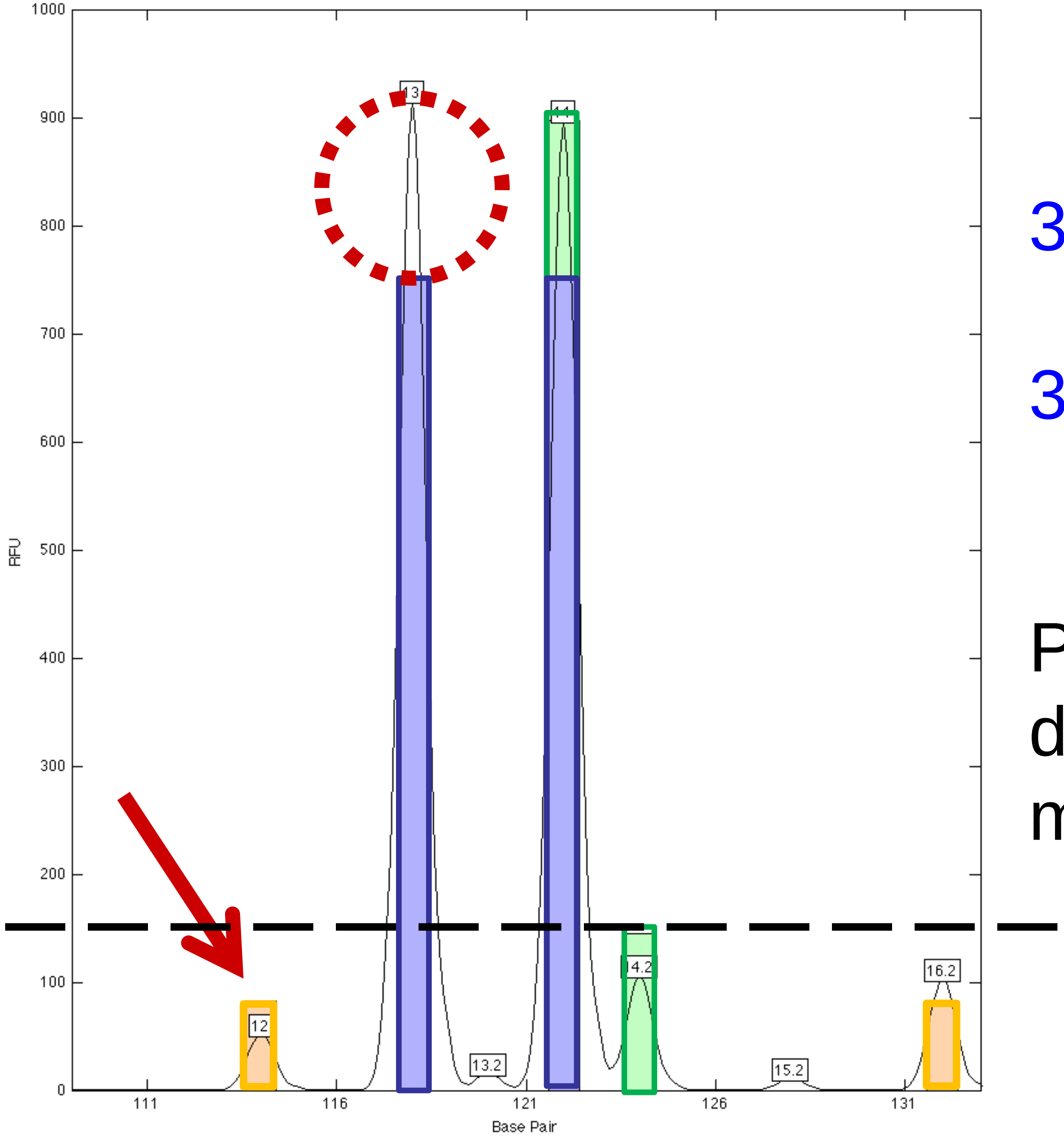
H_D

Combined LR = 5.6 Quintillion

			Genotype Probability Distribution			Weighted Likelihood		Likelihood Ratio	
	allele pair	Likelihood	Questioned	Reference	Suspect	Numerator	Denominator	LR	log(LR)
locus	x	l(x)	q(x)	r(x)	s(x)	l(x)*s(x)	l(x)*r(x)		
CSF1PO	11, 12	0.686	0.778	0.1448	1	0.68615	0.1292	5.31	0.725
D13S317	9, 12	1	1	0.0291	1	0.99952	0.02913	34.301	1.535
D16S539	9, 11	0.985	0.995	0.1238	1	0.98451	0.12188	8.036	0.905
D18S51	13, 17	0.999	1	0.0154	1	0.99915	0.01543	64.677	1.811
D19S433	14, 16.2	0.967	0.948	0.012	1	0.96715	0.01222	79.143	1.898
D21S11	28, 30	0.968	0.98	0.0872	1	0.96809	0.08648	11.194	1.049
D2S1338	23, 24	0.998	1	0.0179	1	0.99831	0.01787	55.866	1.747
D3S1358	15, 17	0.988	0.994	0.1224	1	0.98759	0.12084	8.14	0.911
D5S818	11, 11	0.451	0.394	0.0537	1	0.45103	0.07309	6.17	0.79
D7S820	11, 12	0.984	0.978	0.0356	1	0.98383	0.03617	27.198	1.435
D8S1179	13, 14	0.203	0.9	0.1293	1	0.20267	0.02993	6.771	0.831
FGA	21, 25	0.32	0.356	0.028	1	0.31986	0.01906	16.783	1.225
TH01	7, 7	0.887	0.985	0.1739	1	0.88661	0.15588	5.687	0.755
TPOX	8, 8	1	1	0.1375	1	1	0.13746	7.275	0.862
vWA	15, 20	0.998	0.996	0.0057	1	0.99808	0.00569	174.834	2.243

Review of One Replicate (of 50K)

D19S433



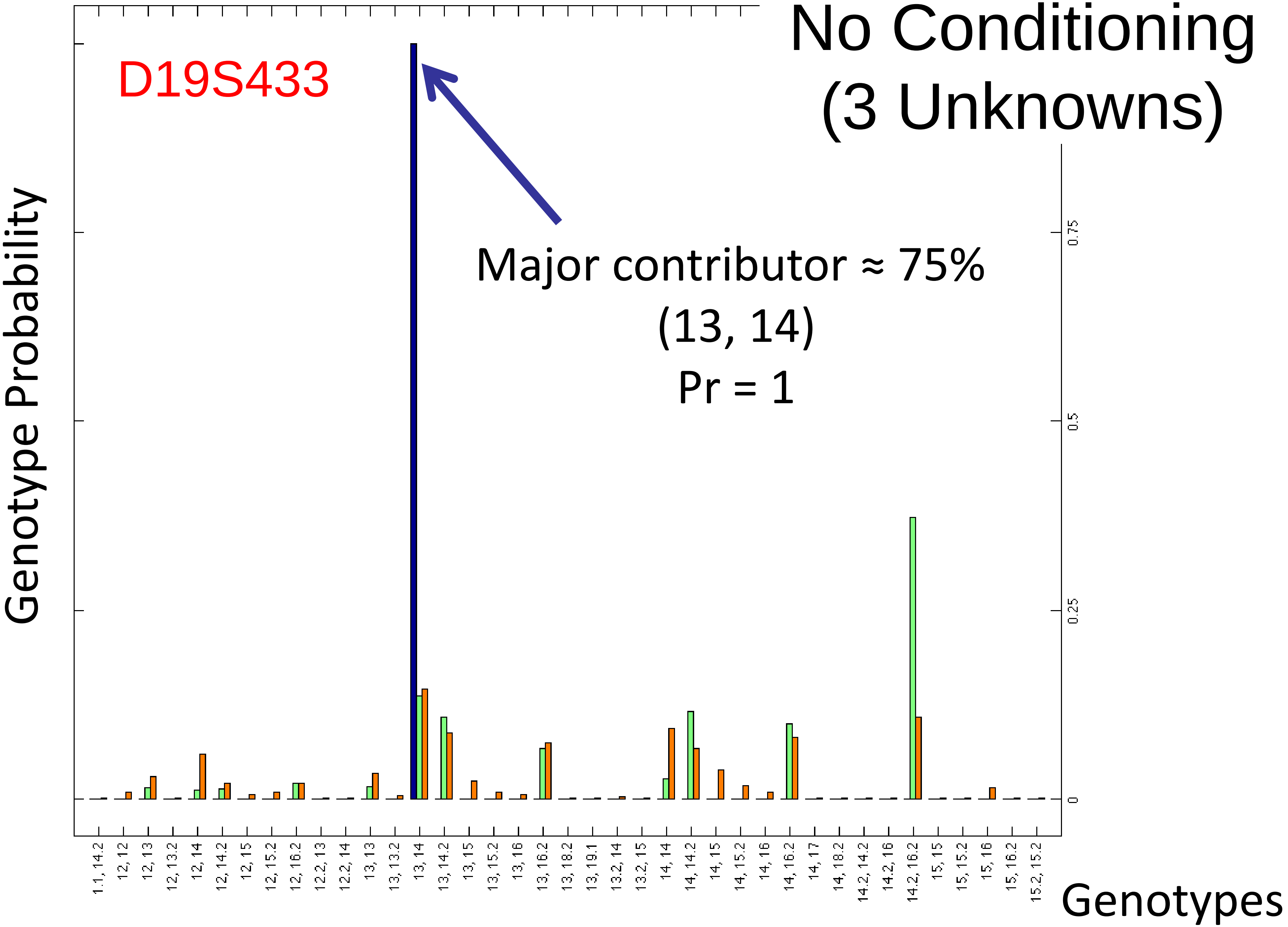
150 RFU

3P mixture,

3 Unknowns

Poor fit of the data to the model

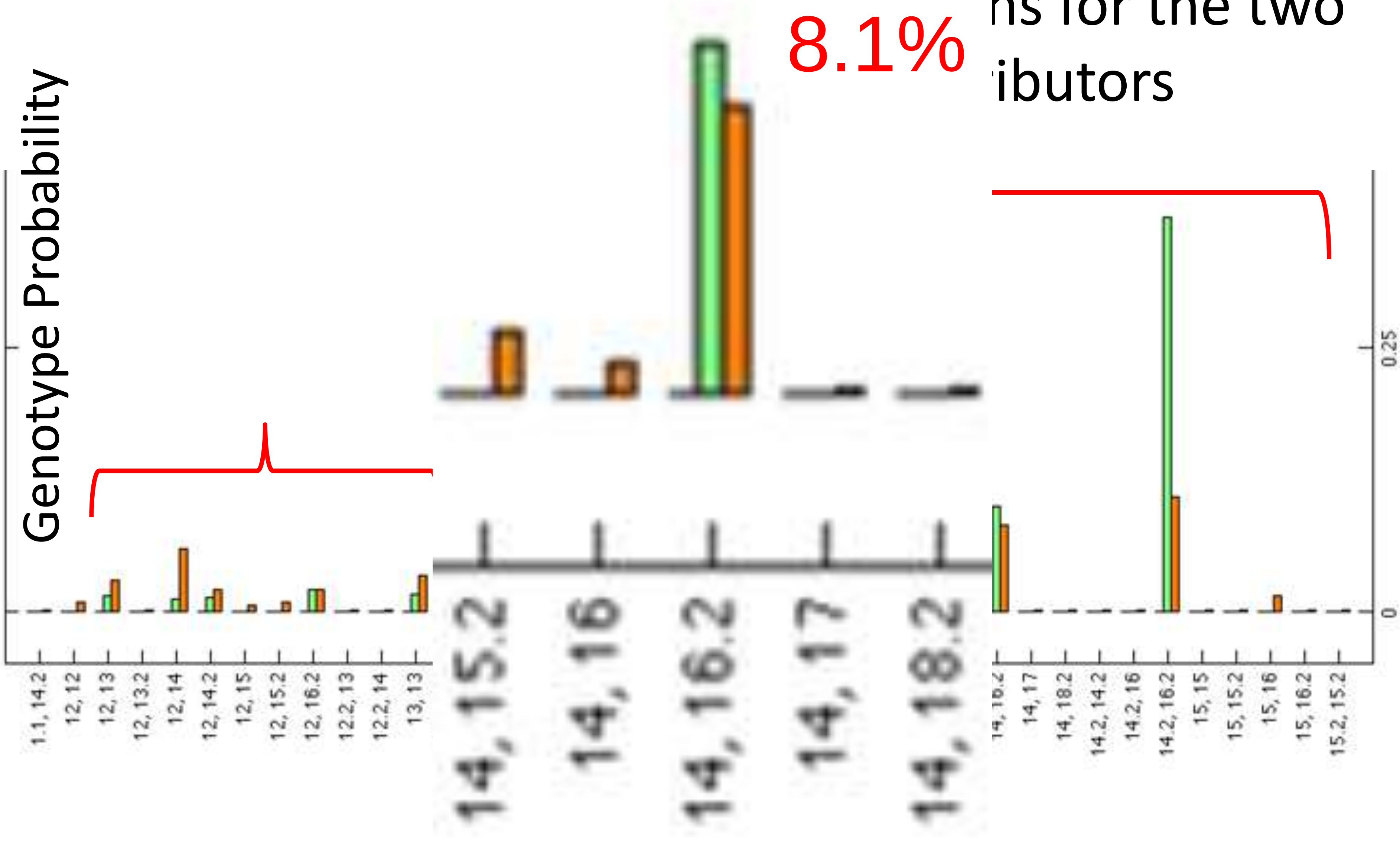
No Conditioning
(3 Unknowns)



Major contributor ≈ 75%
(13, 14)
Pr = 1

No Conditioning (3 Unknowns)

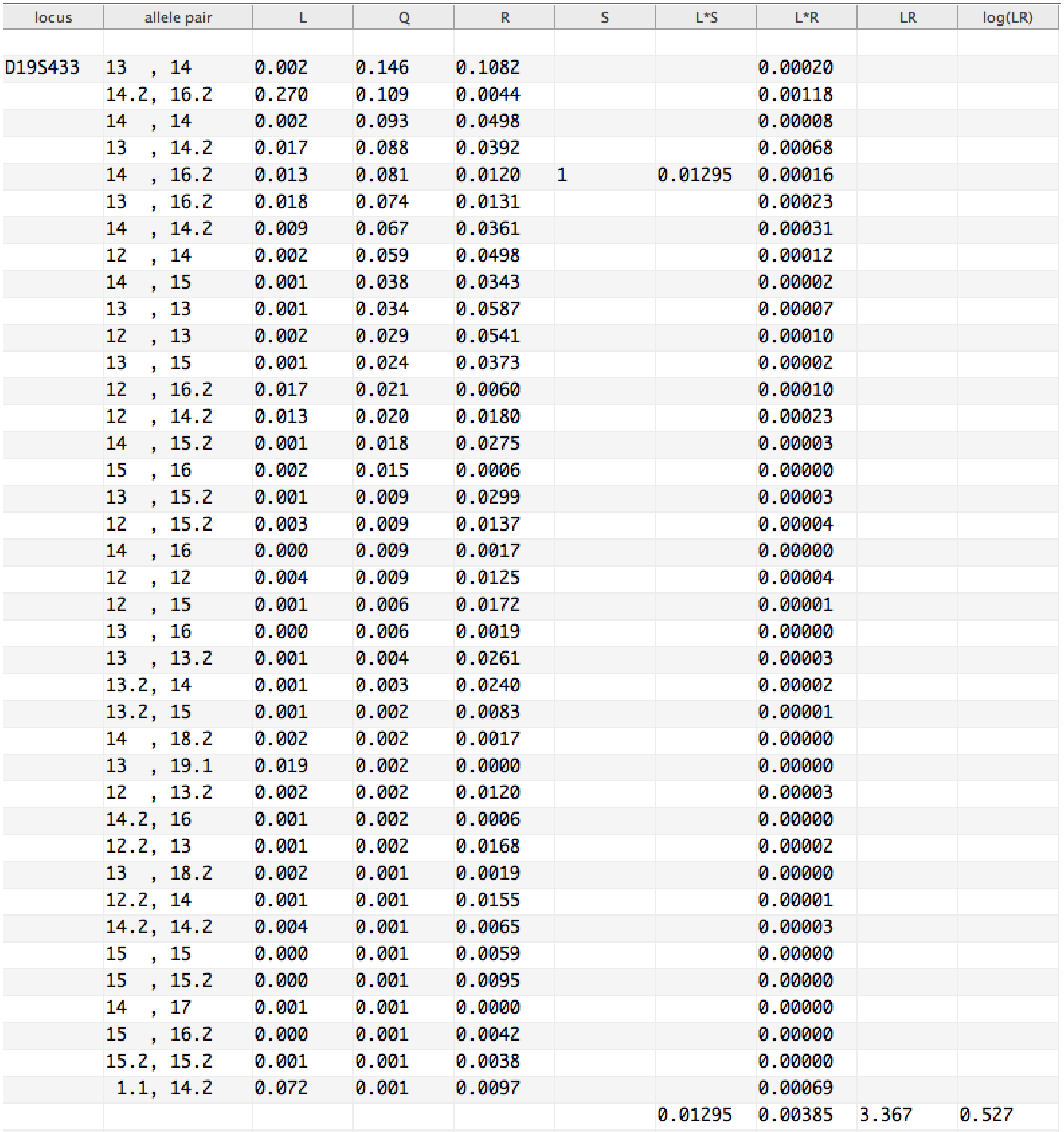
D19S433



8.1%

ns for the two

ibutors



locus	allele pair	L	Q	R	S	L*S	L*R	LR	log(LR)
D19S433	13 , 14	0.002	0.146	0.1082			0.00020		
	14.2, 16.2	0.270	0.109	0.0044			0.00118		
	14 , 14	0.002	0.093	0.0498			0.00008		
	13 , 14.2	0.017	0.088	0.0392			0.00068		
	14 , 16.2	0.013	0.081	0.0120	1	0.01295	0.00016		
	13 , 16.2	0.018	0.074	0.0131			0.00023		
	14 , 14.2	0.009	0.067	0.0361			0.00031		
	12 , 14	0.002	0.059	0.0498			0.00012		
	14 , 15	0.001	0.038	0.0343			0.00002		
	13 , 13	0.001	0.034	0.0587			0.00007		
	12 , 13	0.002	0.029	0.0541			0.00010		
	13 , 15	0.001	0.024	0.0373			0.00002		
	12 , 16.2	0.017	0.021	0.0060			0.00010		
	12 , 14.2	0.013	0.020	0.0180			0.00023		
	14 , 15.2	0.001	0.018	0.0275			0.00003		
	15 , 16	0.002	0.015	0.0006			0.00000		
	13 , 15.2	0.001	0.009	0.0299			0.00003		
	12 , 15.2	0.003	0.009	0.0137			0.00004		
	14 , 16	0.000	0.009	0.0017			0.00000		
	12 , 12	0.004	0.009	0.0125			0.00004		
	12 , 15	0.001	0.006	0.0172			0.00001		
	13 , 16	0.000	0.006	0.0019			0.00000		
	13 , 13.2	0.001	0.004	0.0261			0.00003		
	13.2, 14	0.001	0.003	0.0240			0.00002		
	13.2, 15	0.001	0.002	0.0083			0.00001		
	14 , 18.2	0.002	0.002	0.0017			0.00000		
	13 , 19.1	0.019	0.002	0.0000			0.00000		
	12 , 13.2	0.002	0.002	0.0120			0.00003		
	14.2, 16	0.001	0.002	0.0006			0.00000		
	12.2, 13	0.001	0.002	0.0168			0.00002		
	13 , 18.2	0.002	0.001	0.0019			0.00000		
	12.2, 14	0.001	0.001	0.0155			0.00001		
	14.2, 14.2	0.004	0.001	0.0065			0.00003		
	15 , 15	0.000	0.001	0.0059			0.00000		
	15 , 15.2	0.000	0.001	0.0095			0.00000		
	14 , 17	0.001	0.001	0.0000			0.00000		
	15 , 16.2	0.000	0.001	0.0042			0.00000		
	15.2, 15.2	0.001	0.001	0.0038			0.00000		
	1.1, 14.2	0.072	0.001	0.0097			0.00069		
						0.01295	0.00385	3.367	0.527

Suspect "A"
Genotype

39 probable
genotypes

D19S433

Suspect A = 14, 16.2

$H_P = 0.013$

Allele Pair	Probability	Genotype Frequency	Prob * GenFreq
13,14	0.002	0.1082	0.00020
14.2, 16.2	0.270	0.0044	0.00118
14, 14	0.002	0.0498	0.00008
13, 14.2	0.017	0.0392	0.00068
14, 16.2	0.013	0.0120	0.00016
13, 16.2	0.018	0.0131	0.00023
etc…	etc…	etc…	etc…
		Sum	**0.00385**

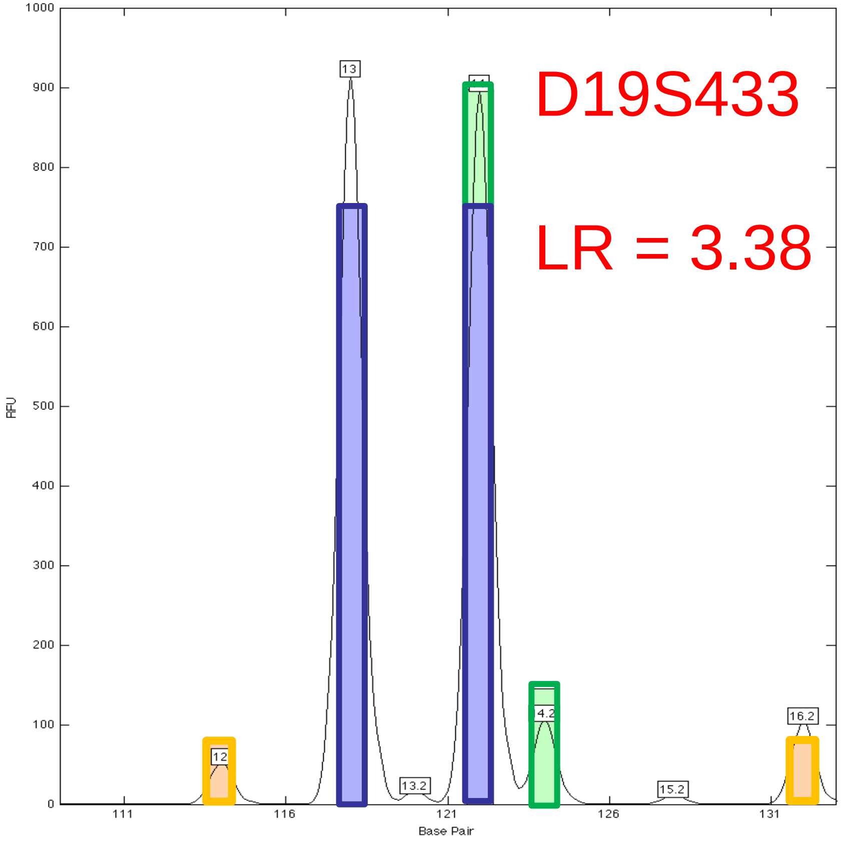
H_D

$$LR = \frac{0.013}{0.00385} = 3.38$$

D19S433

No Conditioning (3 Unknowns)

No Conditioning



D19S433

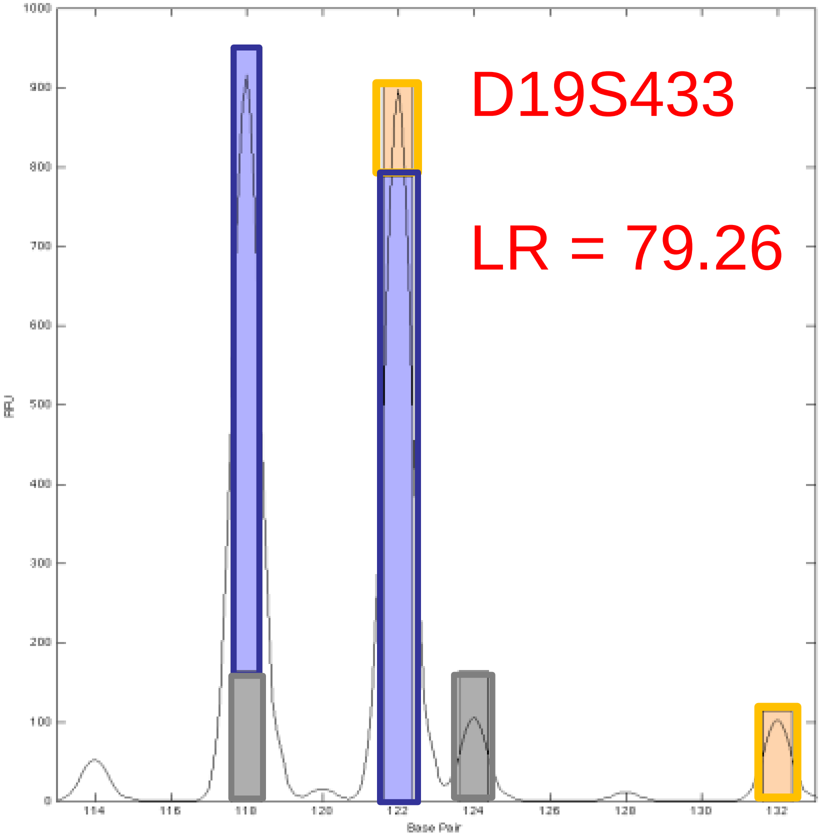
LR = 3.38

Profile - Combined log(LR)

Suspect A log(LR) = 8.03

Suspect B log(LR) = 7.84

Conditioned on Victim



D19S433

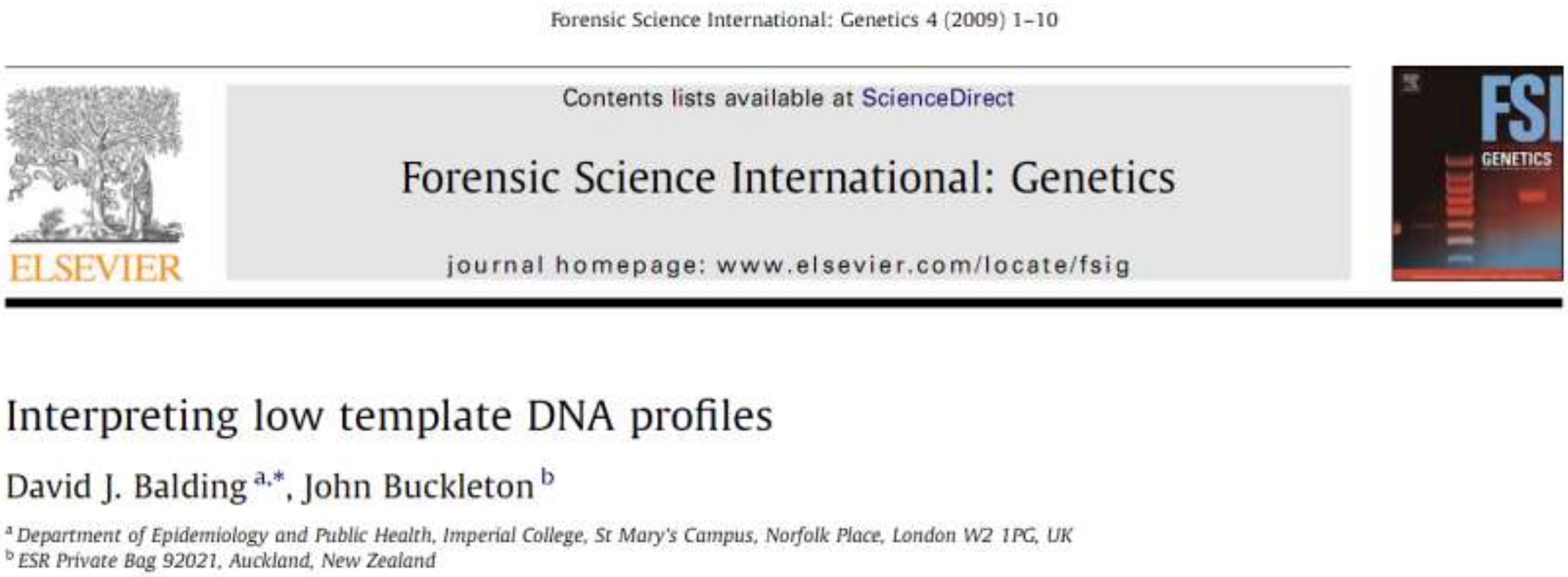
LR = 79.26

Profile - Combined log(LR)

Suspect A log(LR) = 18.72

Suspect B log(LR) = 19.45

LR with Pr(Drop-out)



Forensic Science International: Genetics 4 (2009) 1–10

Contents lists available at ScienceDirect

Forensic Science International: Genetics

journal homepage: www.elsevier.com/locate/fsig

ELSEVIER

Interpreting low template DNA profiles

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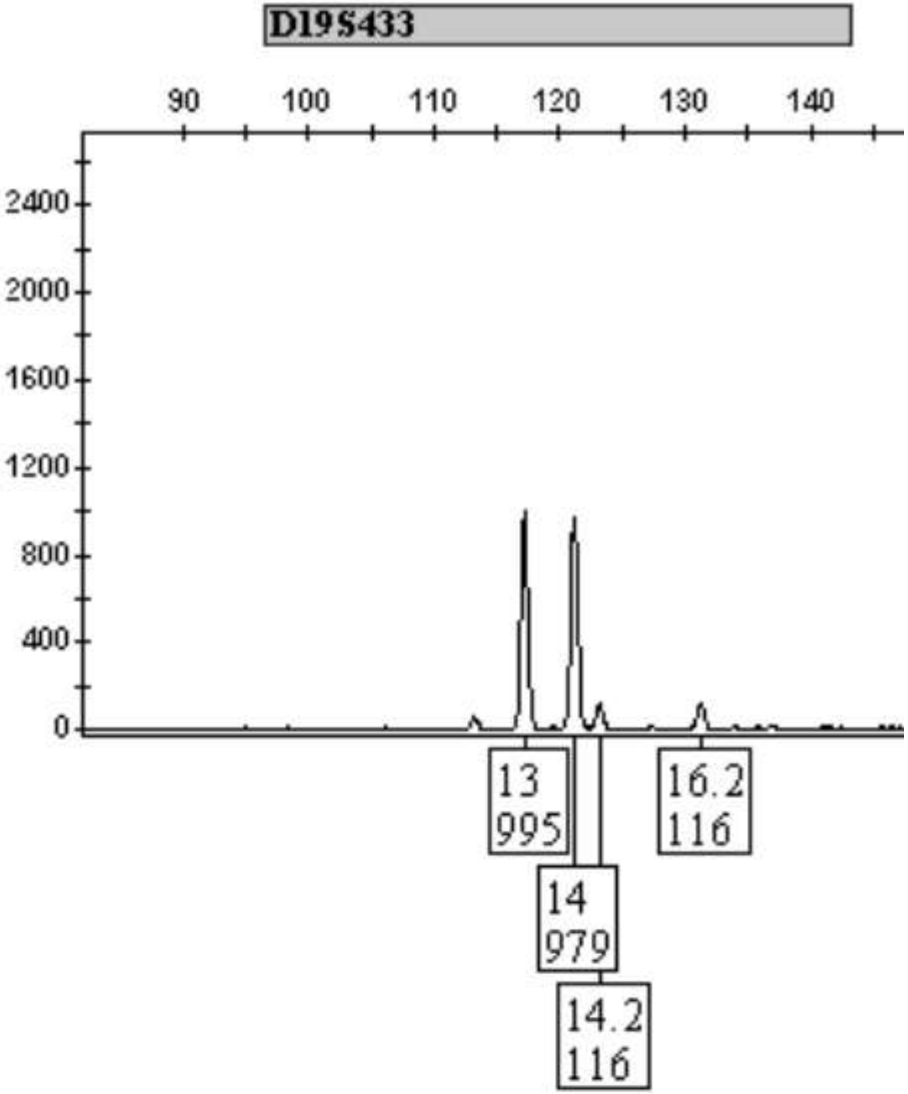
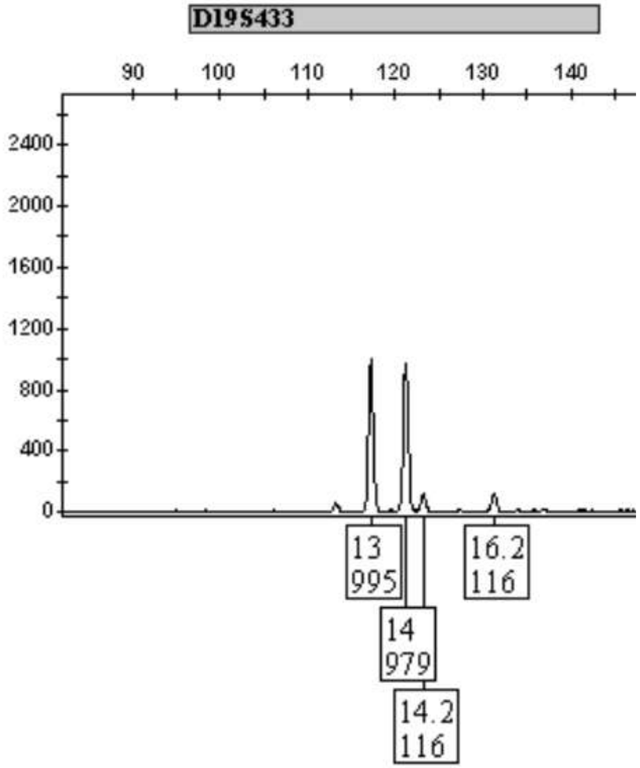
3 Person Mixture



V = 13, 14
CP = 13, 14.2
S = 15, 16.2

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



V = 13, 14
CP = 13, 14.2
S = 15, 16.2

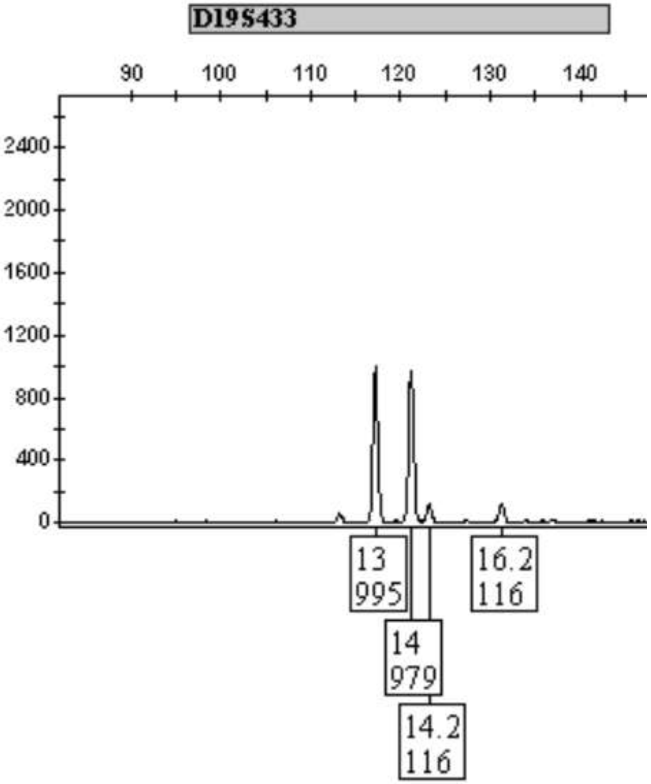
Pr(Drop-out) = 10%
Pr(Drop-in) = 1%

$P(E|H_1)$ = Pr(No Drop-out at 16.2) Pr(Drop-out at 15) Pr(No Drop-in)

= 0.90 0.10 0.99

= 0.0891

3 Person Mixture



V = 13, 14
CP = 13, 14.2
S = 15, 16.2

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

Keith Inman, Norah Rudin and Kirk Lohmueller have modified the Balding program to incorporate your own data for estimating Pr(Drop-out).

Summary of the Issues

- We need to move away from the interpretation of mixtures from an “allele-centric” point of view.
- Methods to incorporate probability will be necessary as we make this transition and confront issues of low-level profiles with drop-out.

- “Just as logic is reasoning applied to truth and falsity, probability is reasoning with uncertainty”

-Dennis Lindley

Summary of the Issues

- The LR is a method to evaluate evidence that can overcome many of the limitations we are facing today.
- This will require (obviously) software solutions… however, we need to better understand and be able to explain the statistics as a community.
- “But, for my own part, it was Greek to me”
  - — William Shakespeare, *Julius Caesar*
- “We know what we are, but know not what we may be.” — William Shakespeare, *Hamlet*

Summary of the Issues

- Extensive training will be necessary – and a single 8 hour workshop will once a year will not suffice. As Robin stated, these are quick fixes for a larger learning gap.
- “Do, or do not. There is no try.”
  — Yoda

Thank You

- “I can no other answer make but thanks, and thanks.” - William Shakespeare, *Twelfth Night*

http://es.wikipedia.org/wiki/William_Shakespeare

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Charlotte Word
John Butler

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