

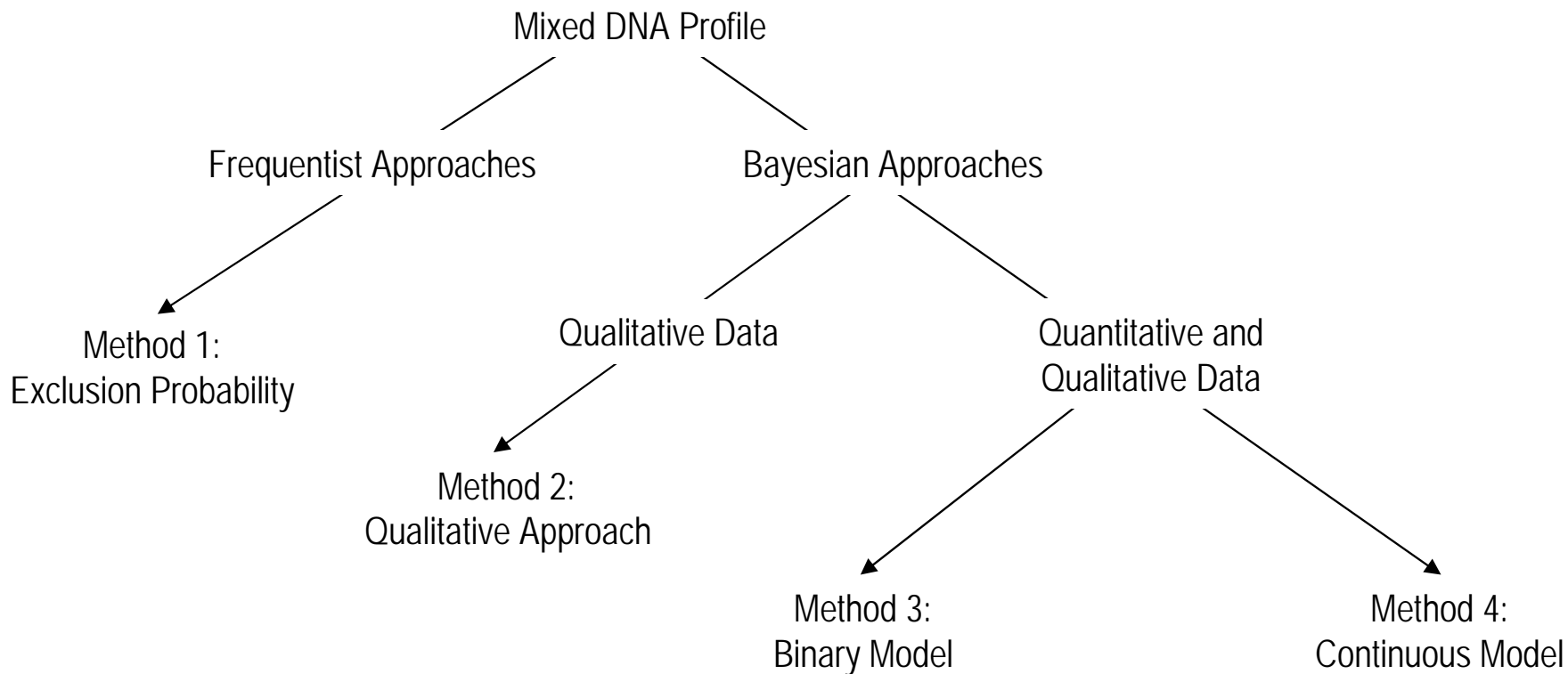
Mixtures

DNA Statistics Workshop

ISFG

2007





Methods used in the interpretation of mixtures.



	Number of alleles showing					
	1	2	3	4	5	6
D3	0.00	0.05	0.37	0.46	0.12	0.00
VWA	0.00	0.04	0.20	0.47	0.10	0.00

This has been
a major issue in some Australian cases

D18	0.00	0.01	0.11	0.39	0.40	0.10
D19	0.00	0.08	0.35	0.40	0.15	0.01
THO	0.00	0.07	0.40	0.44	0.09	0.00
FGA	0.00	0.01	0.14	0.42	0.35	0.07

The proportion of three person mixtures that would present four or fewer alleles for the SGM⁺™ is 0.033.

The result for the Profiler Plus™ loci was 0.062



Simon Walsh AFP

James Curran AU

“Exclusion” type approaches

- Random man not excluded/included
- Conditional random man not excluded
- One of the preferred choices in the US
- DAB draft
- “PE provides an estimate of the portion of the population that has a genotype comprising of an allele or alleles not observed in the mixed profile”

Probability of exclusion

- the exclusion probability at this locus (PE_l) is

$$PE_l = 1 - \left(\sum_{i=1}^n p(A_i) \right)^2$$

- assuming Hardy-Weinberg equilibrium
- The PE across multiple loci (PE) is calculated as

$$PE = 1 - \prod_l (1 - PE_l)$$



Locus 1	Locus 2
abc	de

Allele	Allele probability
a	0.10
b	0.12
c	0.08
d	0.13
e	0.10

	Locus 1	Locus 2	
	abc	de	
$\sum_i \Pr(A_i)$	0.30 ↓	0.23 ↓	
$1 - \left(\sum_i \Pr(A_i) \right)^2$	0.91 ↓	0.9471 ↓	0.995239 =CPE ↑
1-PE = PI	0.09	0.0529	0.004761 = CPI

Locus 1	Locus 2
abcd	efg

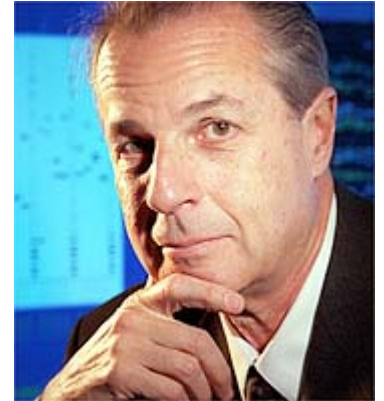
Allele	Allele probability
a	0.10
b	0.12
c	0.08
d	0.13
e	0.10
f	0.12
g	0.25

Probability of exclusion

- “Not as powerful as LR”
- Bruce Budowle 2001
- Some people like the idea that it does not assume the number of contributors in the mixture
- What is the proper place for it in mixture analysis?
Has it still got a place?



Probability of exclusion – Brenner's point



- A Alleles in mixture
 - B Genotype of suspect
 - C Suspect is not excluded
-
- Can you work out C from A & B?
 - Can you work out B from A & C?

Parameters heterozygous balance and stutter

- Two definitions
- Consider the total area of the allelic products, ϕ_A , associated with an allele at a locus. We sum the areas for the $n+1$ and n bands and $(n-4)$ stutter allele (ϕ_S). $n-8$ and other stutter bands are ignored.

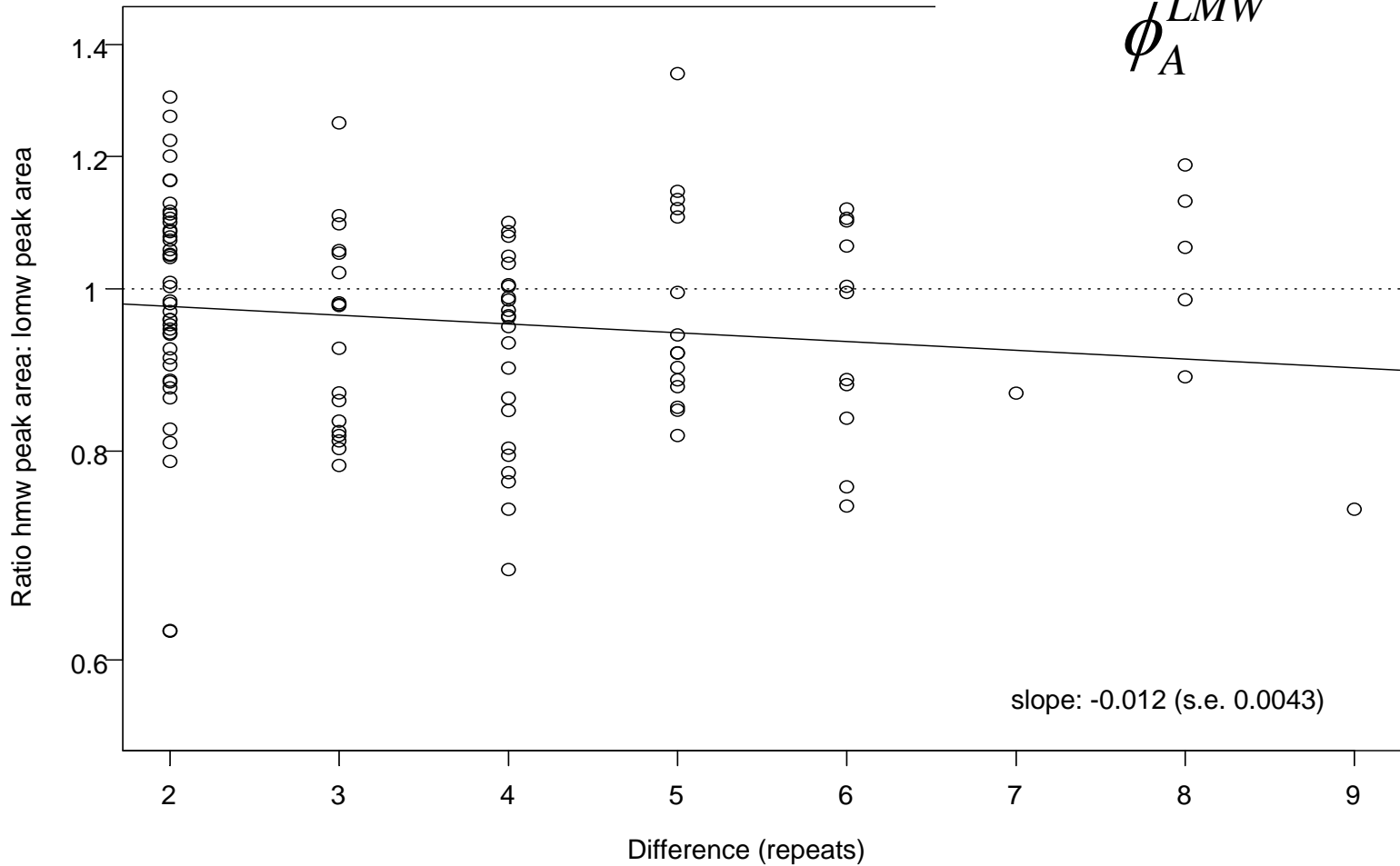
$$Hb = \frac{\phi_A^{HMW}}{\phi_A^{LMW}}$$

$$Hb = \frac{\phi_A^{smaller}}{\phi_A^{larger}}$$



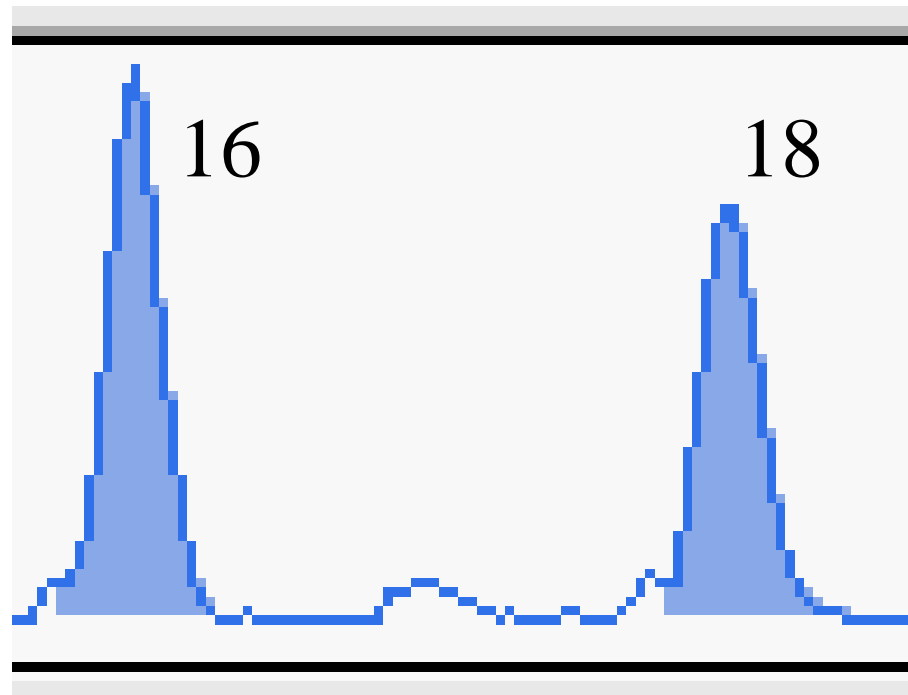
D18

$$0.6 \leq \frac{\phi_A^{HMW}}{\phi_A^{LMW}} \leq 1.66$$



Typical heterozygote imbalance

- General guideline - $0.6 \leq \frac{\phi_{N\&N+1}^{HMW}}{\phi_{N\&N+1}^{LMW}} \leq 1.66$



Stepwise implementation of the binary approach

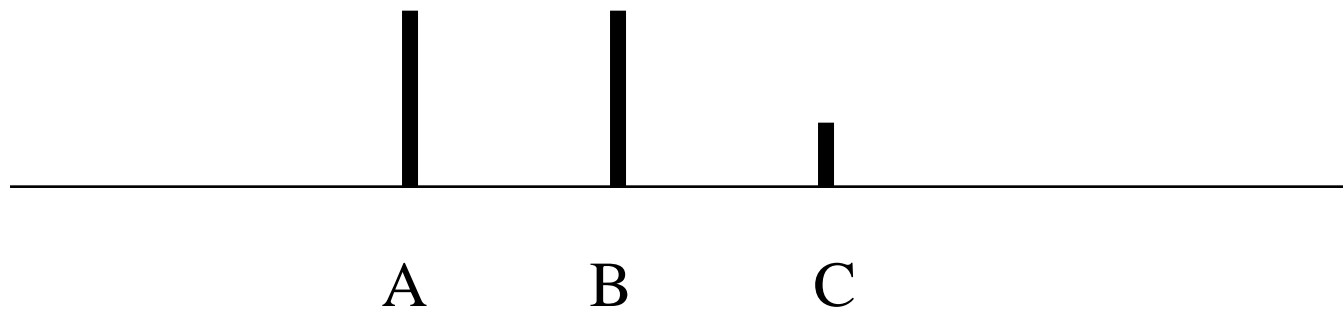
- Hypothesis formation and # of contributors
- Is there a conditioning profile (take care with the word “conditioning”)
- Assignment of possible combinations
- Determination of “who is behind the bar”
- Calculation of the LR



Consider

- Victim(V) AB
- Suspect(S) CC
- Stain is ABC

Victim states that she was raped by one man and has no consensual partners. Intimate sample.



Set up the Hypotheses

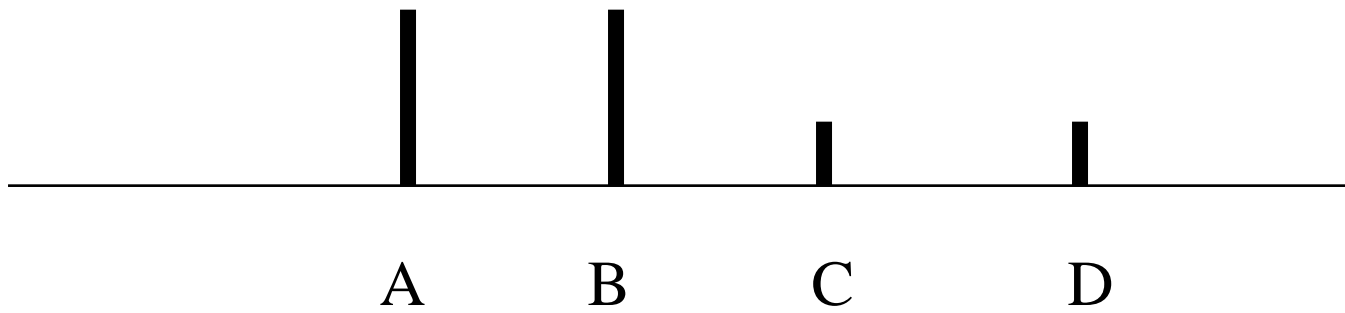
- H_p : The stain contains the DNA of the suspect and the victim
- H_d : The stain contains the DNA of the the victim and a random person



Mixtures

- $p(E|H_p)=1$
- Given H_d
- the true offender could be AC, BC, or CC

To try



$V=AB$

$S=CD$

Combinations without area

- Please write out all the combinations for a two person mixture.
- Assume allelic dropout is not an issue.
- Four peak locus
- Three peak locus
- Two peak locus
- One peak locus



Combinations without area

- Four peak locus
- ABCD
- 6 combinations
- 3 pairs

RM1	RM2
AB	CD
AC	BD
AD	BC
BC	AD
BD	AC
CD	AB

Combinations without area

- Three peak locus ABC
- 12 combinations

RM1	RM2
AA	BC
BB	AC
CC	AB
AB	AC
AB	BC
AC	BC

RM1	RM2
BC	AA
AC	BB
AB	CC
AC	AB
BC	AB
BC	AC

Combinations without area

- Two peak locus AB
- 7 combinations

RM1	RM2
AA	BB
AB	BB
AB	AA
AB	AB

RM1	RM2
BB	AA
BB	AB
AA	AB

Combinations without area

RM1	RM2
AA	AA

- One peak locus A
- 1 combination



Eliminating Combinations with area

- Provisional rules
- Four peak locus
- ABCD
- For each het
- Simple het guideline

$$0.6 \leq \frac{\phi_1}{\phi_2} \leq 1.66$$

RM1	RM2
AB	CD
AC	BD
AD	BC
BC	AD
BD	AC
CD	AB

Eliminating Combinations with area

- Three peak locus
- ABC
- For each het

RM1	RM2
AA	BC
BB	AC
CC	AB
AB	AC
AB	BC
AC	BC

$$0.6 \leq \frac{\phi_1}{\phi_2} \leq 1.66$$

Shared het guideline

$$0.6 \leq \frac{\phi_s}{\phi_2 + \phi_3} \leq 1.66$$

Shared allele

Eliminating Combinations with area

- Two peak locus AB
- 7 combinations

Het Hom guideline

$$0.6 * \phi_1 \leq \phi_s$$

Simple het guideline

$$0.6 \leq \frac{\phi_1}{\phi_2} \leq 1.66$$

RM1	RM2
AA	BB
AB	BB
AB	AA
AB	AB

Eliminating combinations

- What is left?
- Calculate Mx for each combination

Eliminating Combinations with area 4 peak loci

$$\hat{M}_x = \frac{\phi_1 + \phi_2}{\phi_1 + \phi_2 + \phi_3 + \phi_4}$$

$$1 - \hat{M}_x = \frac{\phi_3 + \phi_4}{\phi_1 + \phi_2 + \phi_3 + \phi_4}$$

RM1	RM2
AB	CD
AC	BD
AD	BC
BC	AD
BD	AC
CD	AB

Eliminating Combinations with area 3 peak loci

$$\hat{M}_x = \frac{\phi_{Hom}}{\phi_{Hom} + \phi_2 + \phi_3}$$

$$\hat{M}_x = \frac{\phi_1 + \phi_2}{\phi_1 + \phi_2 + \phi_{Hom}}$$

$$\hat{M}_x = \frac{\phi_{UL}}{\phi_{UL} + \phi_{UR}}$$

RM1	RM2
AA	BC
BB	AC
CC	AB
BC	AA
AC	BB
AB	CC
AB	BC

Eliminating Combinations with area 2 peak loci

$$\hat{M}_x = \frac{\phi_L}{\phi_L + \phi_R}$$

$$\hat{M}_x = \frac{2\phi_U}{\phi_U + \phi_S}$$

No info

RM1	RM2
AA	BB
AB	BB
AB	AA
AB	AB

Eliminating combinations

- What is left?
- Calculate M_x for each combination
- Are any combinations inconsistent on the basis of M_x ?
- At the moment this relies on the judgement and experience of the RO
- We may be able to make a guideline from further data analysis being planned – currently ± 0.35 -
Amanda Kirkham

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VWA	0.00	0.04	0.29	0.47	0.19	0.02
D16	0.00	0.09	0.40	0.41	0.10	0.01
D2	0.00	0.01	0.10	0.39	0.39	0.11
D8	0.00	0.04	0.26	0.44	0.24	0.03
D21	0.00	0.02	0.19	0.43	0.30	0.06
D18	0.00	0.01	0.11	0.39	0.40	0.10
D19	0.00	0.08	0.35	0.40	0.15	0.01
THO	0.00	0.07	0.40	0.44	0.09	0.00
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“conclusion”

- Dear colleagues I just had not written this bit when they printed the handouts. Actually perhaps that is something we could work on developing together. This probably is the “cutting edge” of mixtures
- # of contributors
- 3 or more persons
- Uncertainty in the #



End

