Reliable Interpretation of Stochastic DNA Evidence

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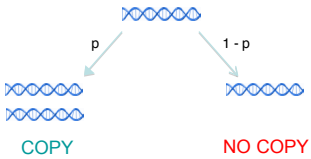
Cybergenetics

Coping with uncertainty

- Reproducible DNA data exhibit stochastic variation
- Probability models can capture stochastic effects
- Genotypes inferred from uncertain data are probability distributions (e.g., CPI)

- Science expects us to account for stochastic effects
- The law expects us to testify within our certainty
- The likelihood ratio (LR) *meets both demands*
- The LR expresses genotype uncertainty, reflecting the underlying data uncertainty

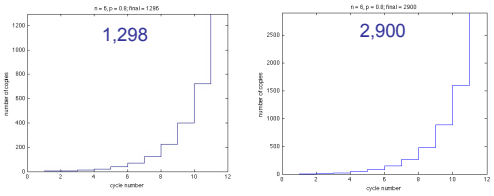
PCR is a random process



PCR efficiency is not 100% efficient. A strand copies with probability *p*, and doesn't copy with probability 1-*p*.

STR peak is a random variable

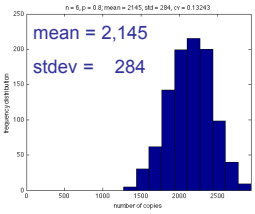
p = 80%, n = 6



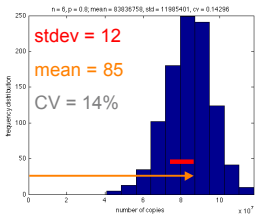
One amplification

Another amplification

STR peak height measurement reflects probability distribution

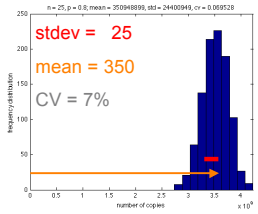


Relative peak certainty: coefficient of variation



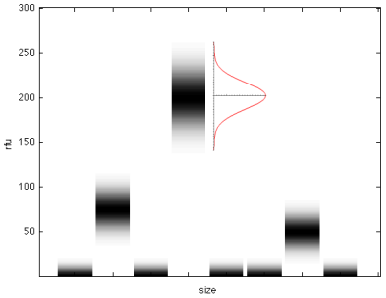
$$CV = \frac{\text{standard deviation}}{\text{mean value}}$$

Four times the peak height, gives twice the peak certainty

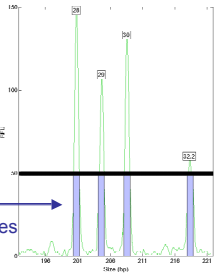


$$CV = \frac{\text{standard deviation}}{\text{mean value}}$$

STR peaks are random variables



To interpret quantitative data, some use a qualitative threshold

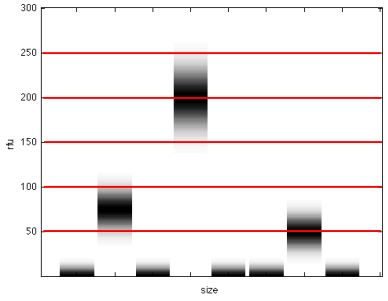


list of included alleles

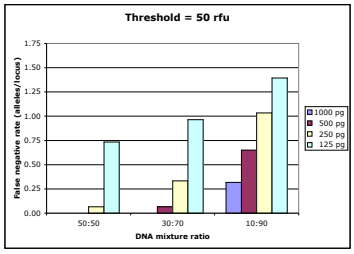
Over threshold, peaks are treated as allele events.

Under threshold, alleles do not exist.

Thresholds introduce error

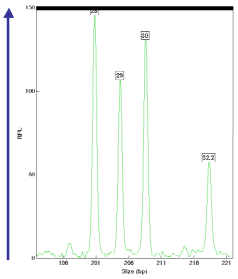


False allele exclusions



2010 SWGDAM Guidelines

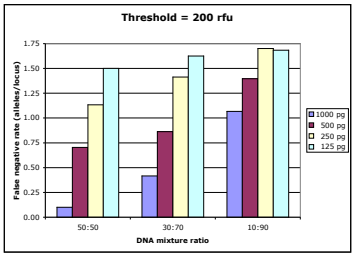
Raising the stochastic threshold.



When every peak is under threshold, all the data disappears.

No genotype, no match score, nothing left to say.

Higher false exclusion rate



SWGDAM 2010 – Mixtures

3.2.2. If a stochastic threshold based on peak height is *not used* in the evaluation of DNA typing results, the laboratory must establish alternative criteria (e.g., quantitation values or use of a probabilistic genotype approach) for addressing potential stochastic amplification. The criteria must be supported by *empirical data and internal validation* and must be documented in the standard operating procedures.

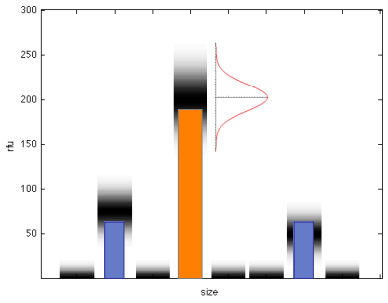
- higher peak threshold discards information
- probability modeling preserves information

Probability modeling

- Bayes Theorem: addresses scientific uncertainty
- uses likelihood function to update probability
- joint likelihood combines independent evidence

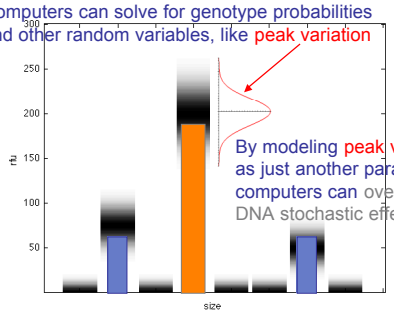
- likelihood: how well parameters explain the data
- STR data: must explain every peak (all rfu)
- likelihood gives probability at one peak:
  genotype allele prediction vs. peak height
- joint likelihood at all peaks:
  multiply together the individual peak likelihoods

Compare genotype pattern vs. data



Overcome stochastic effects

Computers can solve for genotype probabilities and other random variables, like peak variation



By modeling peak variation as just another parameter, computers can overcome DNA stochastic effects

TrueAllele® Casework

- quantitative computer interpretation
- statistical search of probability model
- preserves all identification information
- objectively infer genotype, then match

- any number of mixture contributors
- stutter, imbalance, degraded DNA
- calculates uncertainty of every peak

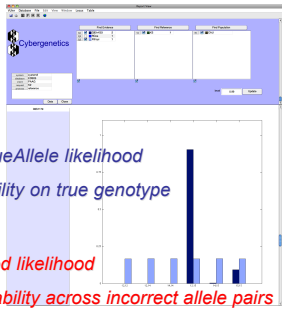
- created in 1999, now in version 25
- used on 100,000 evidence samples
- available as product, service or both

Commonwealth v. Foley

Score	Method
13 thousand	inclusion
23 million	obligate allele
189 billion	TrueAllele

- peak threshold discards information
- probability modeling preserves information

Likelihood Comparison



Quantitative TrueAllele likelihood

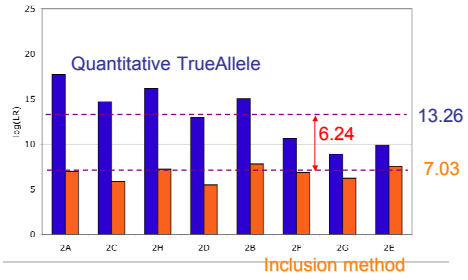
focuses probability on true genotype

Inclusion method likelihood

disperses probability across incorrect allele pairs

MW Perlin, MM Legler, CE Spencer, JL Smith, WP Allan, JL Belrose, BW Duceman. Validating Trueallele DNA Mixture Interpretation. Journal of Forensic Sciences, 2011.

Preserve vs. Discard



SWGDAM 2010 – Mixtures

3.4.3.1. If composite profiles (i.e., generated by combining typing results obtained from multiple amplifications and/or injections) are used, the *laboratory should establish guidelines* for the generation of the composite result. When separate extracts from different locations on a given evidentiary item are combined prior to amplification, the resultant DNA profile is not considered a composite profile. Unless there is a reasonable expectation of sample(s) originating from a common source (e.g., duplicate vaginal swabs or a bone), allelic data from separate extractions from different locations on a given evidentiary item should not be combined into a composite profile. The *laboratory should establish guidelines* for determining the suitability of developing composite profiles from such samples.

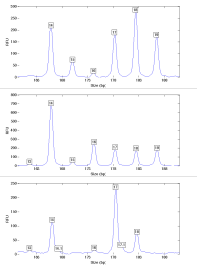
- joint likelihood function combines evidence
- probability modeling preserves information

Regina v. Broughton

- low template mixture
- three DNA contributors
- triplicate amplification
- post-PCR enhancement

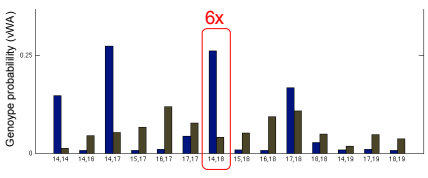
- inconclusive human result
- TrueAllele interpretation

vWA locus data



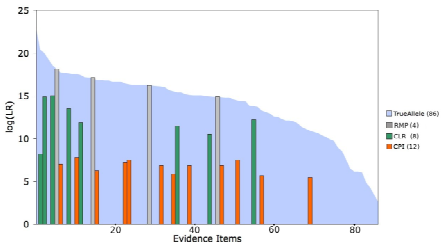
Regina v. Broughton

Score	Method
nothing	human inclusion
3.6 million	TrueAllele computer



- joint likelihood function combines evidence
- probability modeling preserves information

Preserve vs. Discard



- peak threshold discards information - 70% of the time
- quantitative likelihood preserves information - every time

Conclusions

- quantitative data has stochastic effects
- model data with joint likelihood function
- probability modeling preserves information
- and can statistically combine DNA evidence

- exact modeling of peak variation
  can replace inexact thresholds
  to scientifically overcome stochastic effects

Cybergenetics

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