DNA Mixture Interpretation Principles: Observations from a NIST Scientific Foundation Review
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Variation in SOPs Between Forensic Labs

Jennifer Breaux

Senior Forensic Scientist

Montgomery County Police Department

Forensic Biology Unit

Living in a binary world…

- Establish analytical and stochastic thresholds
  - Stochastic threshold as it applies to a mixed sample
- Determine peak height ratio expectations for heterozygous genotypes
  - Vary PHB% based on quality of sample
- Determine the minimum number of contributors to a sample
  - Allele count, PHB%
- Criteria to determine major/minor contributors
  - Mass ratio requirements
- Is the sample suitable for comparisons?
  - Quantitation threshold, minimum # of alleles met, maximum # of contributors
- Is it possible to assume the presence of a contributor to possibly simplify the mixture?
  - When is it appropriate to use FVAs?

Why do we establish all this criteria?

- Main focus is to perform mixture interpretation on a sample to determine the GENOTYPE combinations of possible contributors to that mixed sample
- Interpret these samples prior to comparisons of known samples of individuals except FVAs
  - Can be limiting in a binary world
- Critical to ensure that the statistical approach utilized does NOT drive the interpretation of the sample
  - Conclusions documented prior so appropriate statistic can then be selected

Statistical approaches for a binary world

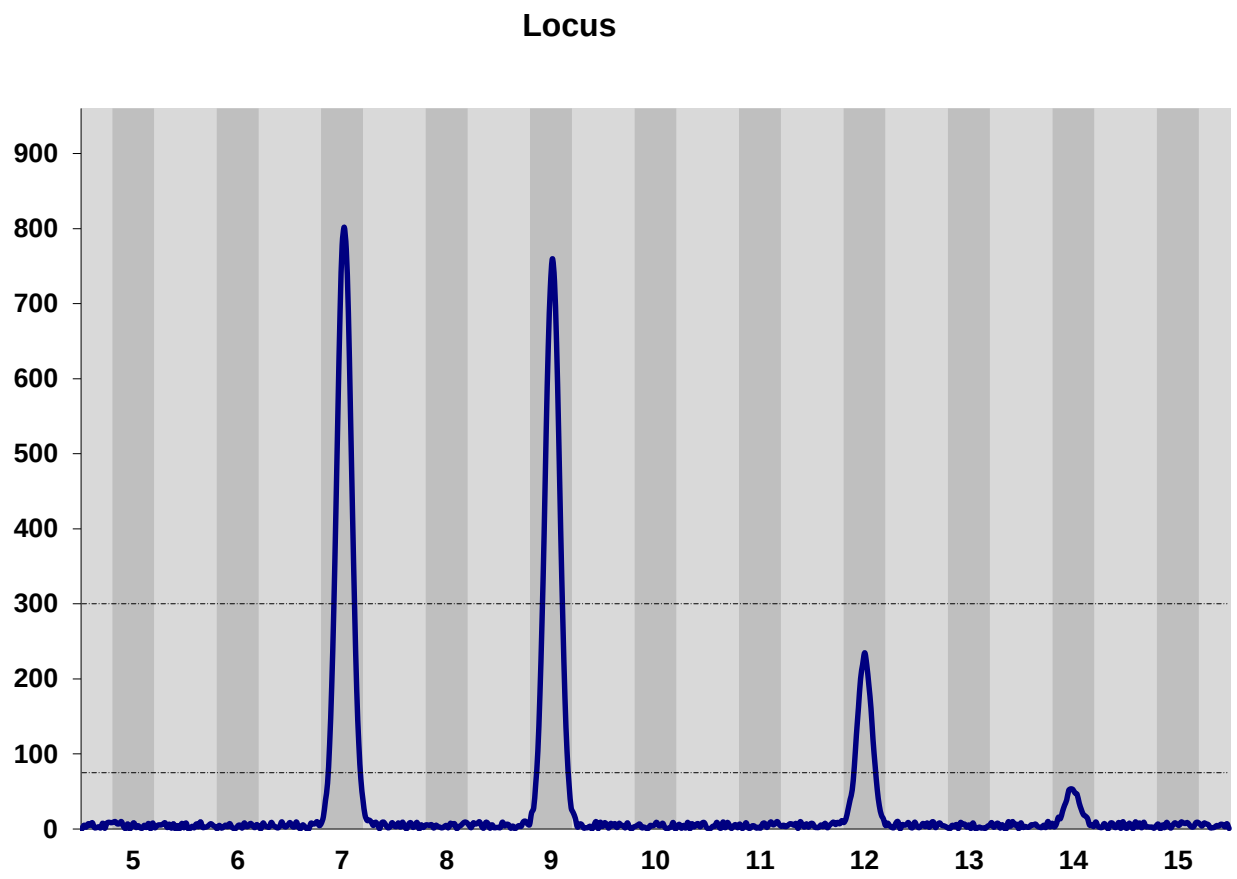
- Provide weight-of-evidence that is appropriate based on the documented interpretation of the sample
- Typically three approaches: random match probability (RMP/mRMP), likelihood ratio (LR) and combined probability of inclusion/exclusion (CPI/CPE)
  - Restricted and unrestricted LRs and CPI
  - Assess for drop out
- Binary approach is limiting so what approach is best suited to tackle complex mixtures?

Moving to a new world…probabilistic genotyping (PG)

- Use of biological modeling, statistical theory, computer algorithms and probability distributions to calculate LRs and/or infer genotypes for the DNA typing results of samples
- Foundation still critical of the binary world concepts (modeling)
- Application to more complex samples that were typically not suitable for comparisons
- Assess weight for possible genotypes instead of a binary approach of allowing all combinations with equal probability
- Semi-continuous and continuous

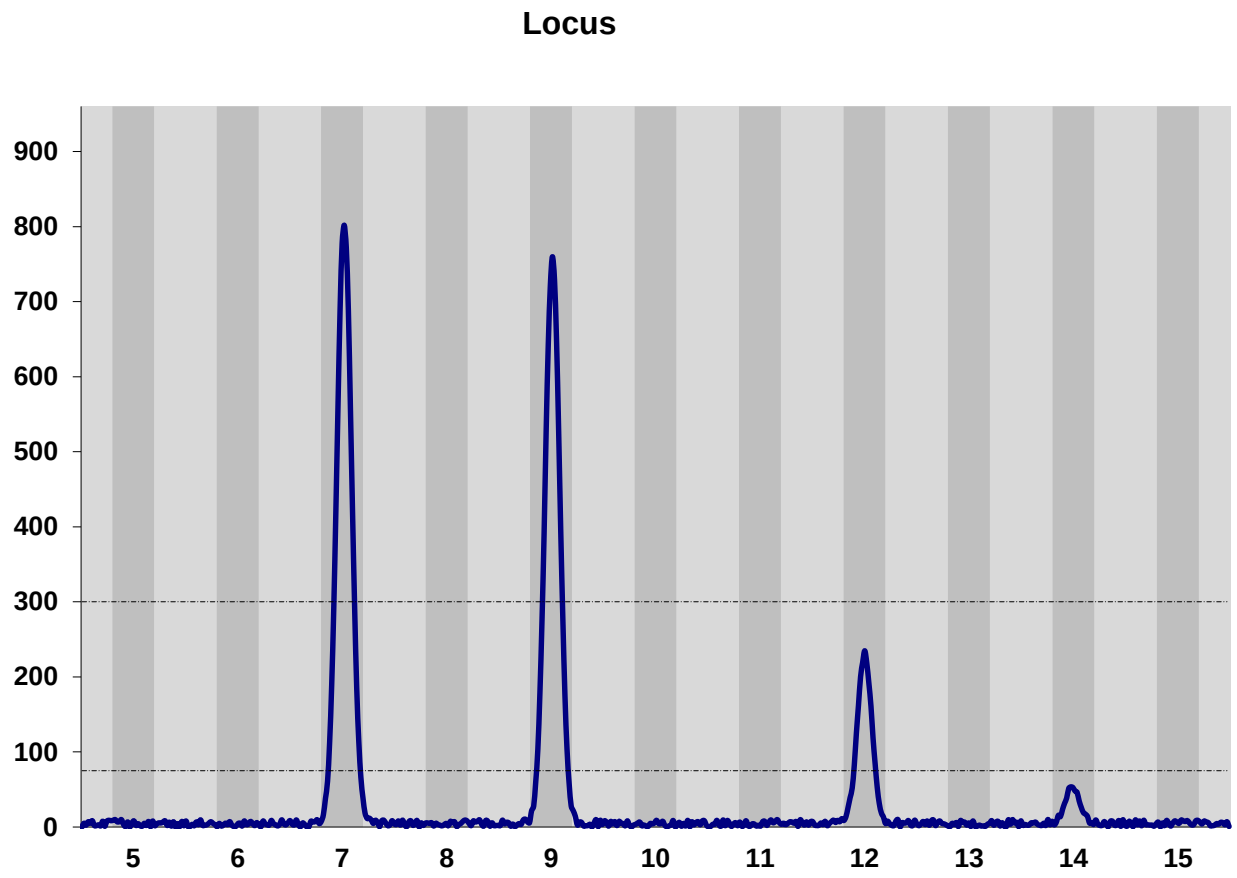
Walk through a one locus example of binary and PG approaches

- AT = 75, ST = 300
- Allele 7 = 800
- Allele ~~8~~ 9 = 750
- Allele 12 = 225
- Allele 14 = 50

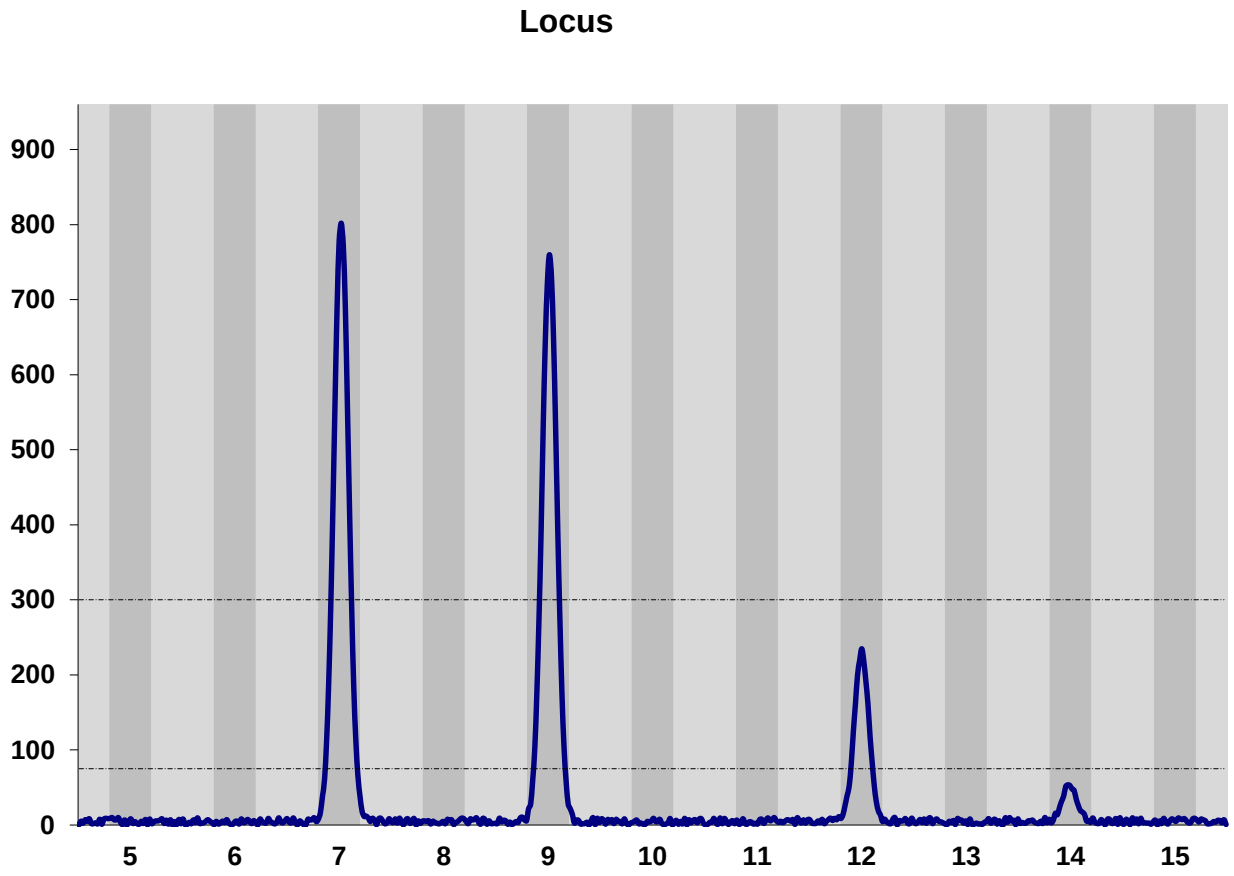


Walk through a one locus example of binary and PG approaches

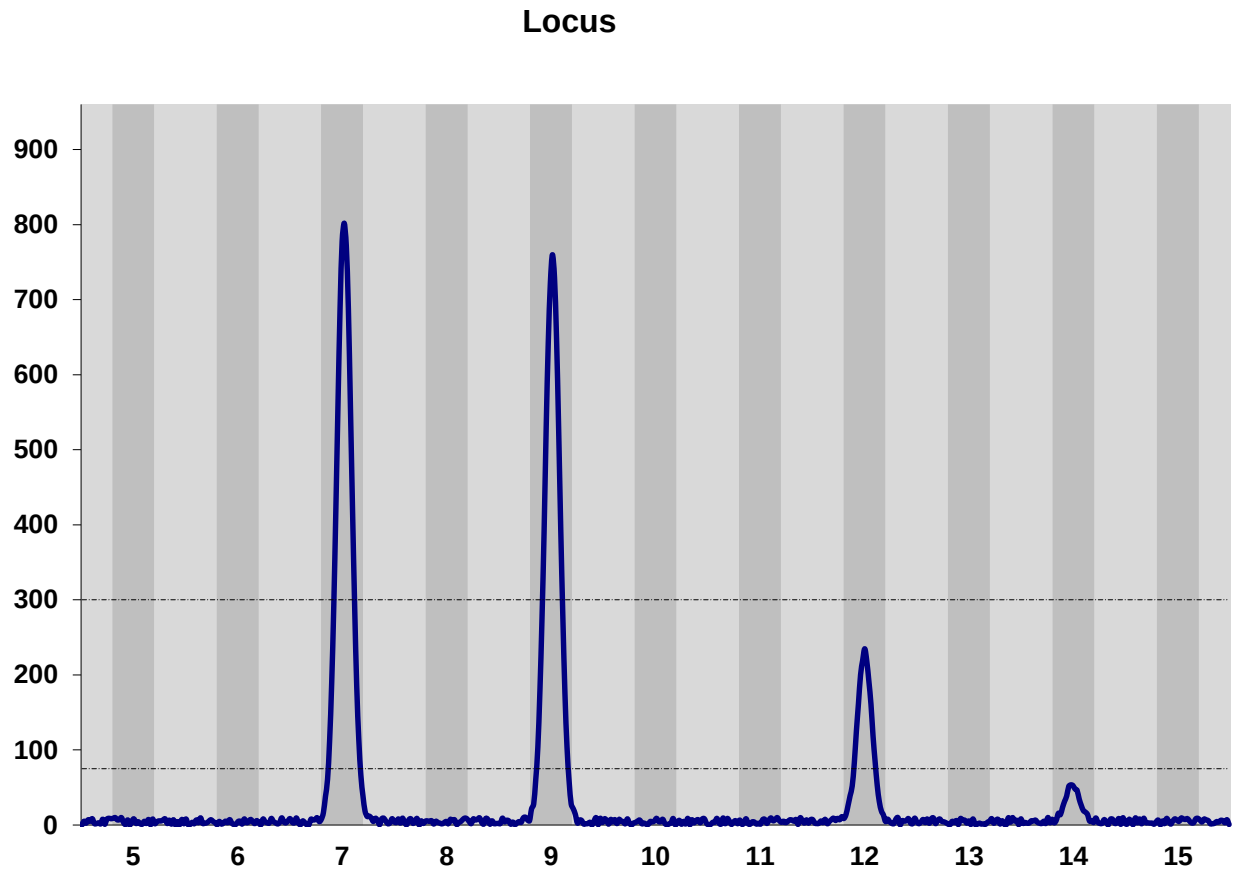
- Call a major?
  - Depends on criteria in your SOPs (3:1, 4:1 etc)



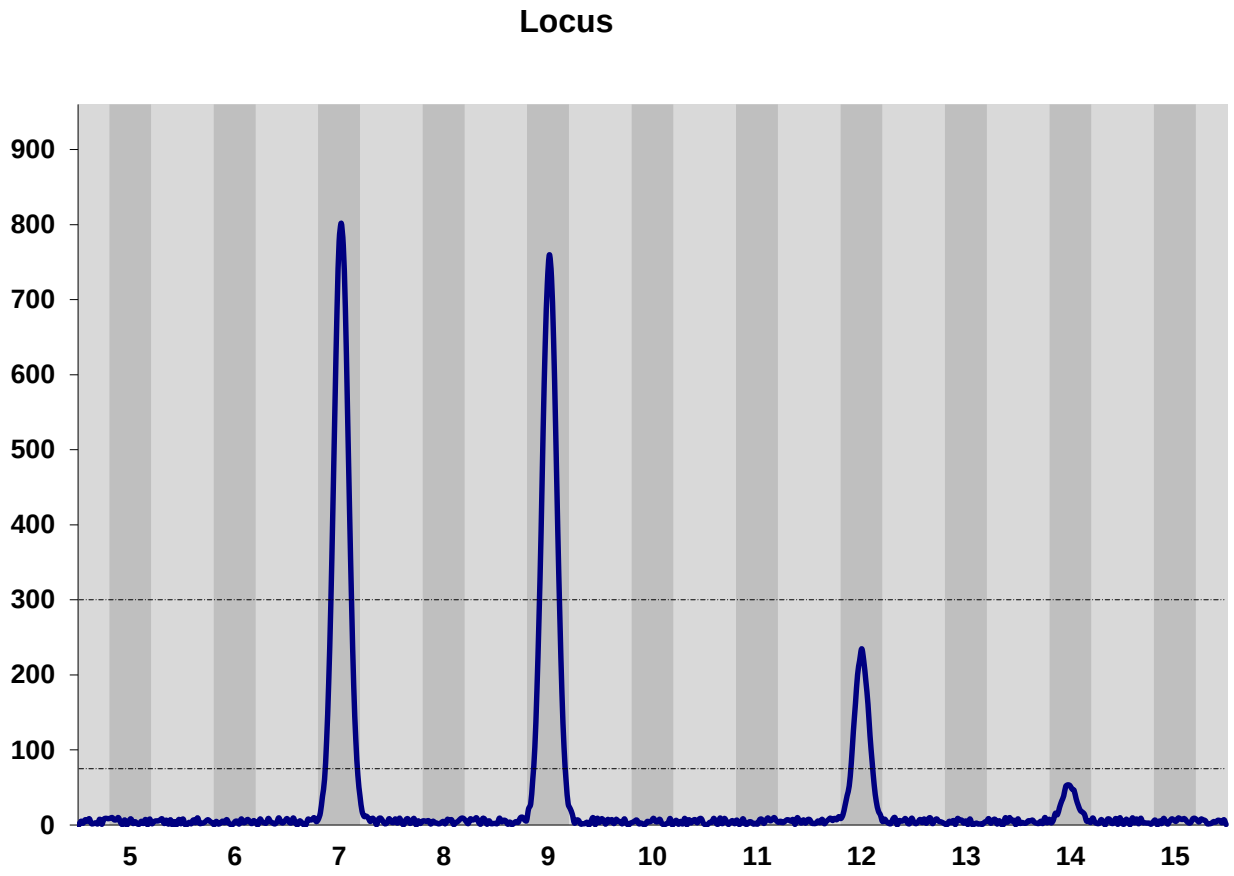
- CPI?
  - Out due to drop-out
- Binary LR?
  - Out unless drop-out allowed
  - No Popstats



- Unrestricted LR without a major
  - Account for drop-out
  - Pairing 7,F and 9,F and 12,F
- Restricted LR with a major
  - Account for drop-out
  - Major 7,9 and minor 12,F



- PG approach using semi-continuous LR
  - Alleles are considered discrete so peak heights may not be used
  - Probability of drop-out and drop-in
- PG approach using continuous LR
  - Alleles are continuous variables
  - Model all aspects of the data present
  - Assess weight to each genotype combinations based on the observed data



Benefits and Difficulties in moving from a binary to PG world

- Benefits
  - Ability to exclude more individuals (More powerful tool for supporting the inclusion of true contributors and the exclusion of false contributors)
  - Utilize all aspects of the data in the interpretation
  - Improved approach by weighting genotype combinations compared to binary
  - Take QUANTITY and QUALITY of the mixed sample into consideration when modeling
  - Modeling of low-level data by considering the uncertainty that exists compared to binary methods

Benefits and Difficulties in moving from a binary to PG world

- Difficulties
  - Training
  - Time spent to rein in the subjectivity in the determination of number of contributors especially when using sub-threshold data
  - Determine if data is still too complex for comparisons
  - Explanation in court (multiple combinations of DNA types possible to explain the observed data)
  - Establishing routine methodology to review to scrutinize run outputs prior to comparisons
  - Documentation for case files and technical reviews due to increased volume

Key Takeaways

- Fully document interpretation prior to comparisons
- Statistical method does NOT drive interpretations
- Transition to a model that best utilizes all aspects of the data
- Use our community for help!

Complex mixtures…can you really avoid them?