

Y Chromosome Markers

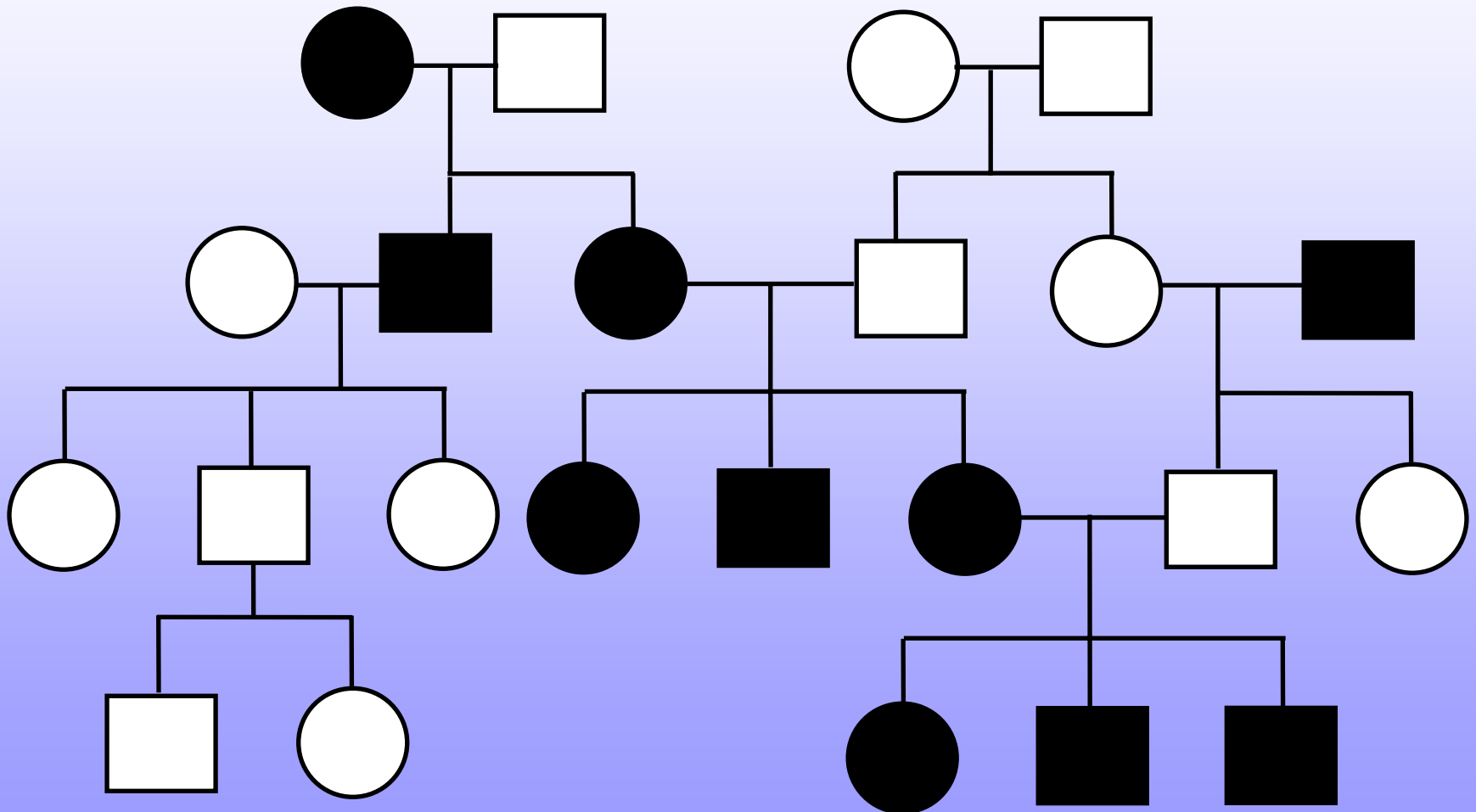
Lineage Markers

- Autosomal chromosomes recombine with each meiosis
- Y and Mitochondrial DNA does not
- This means that the Y and mtDNA remains constant from generation to generation
 - Except for mutations
- Therefore Y and mtDNA are known as lineage markers

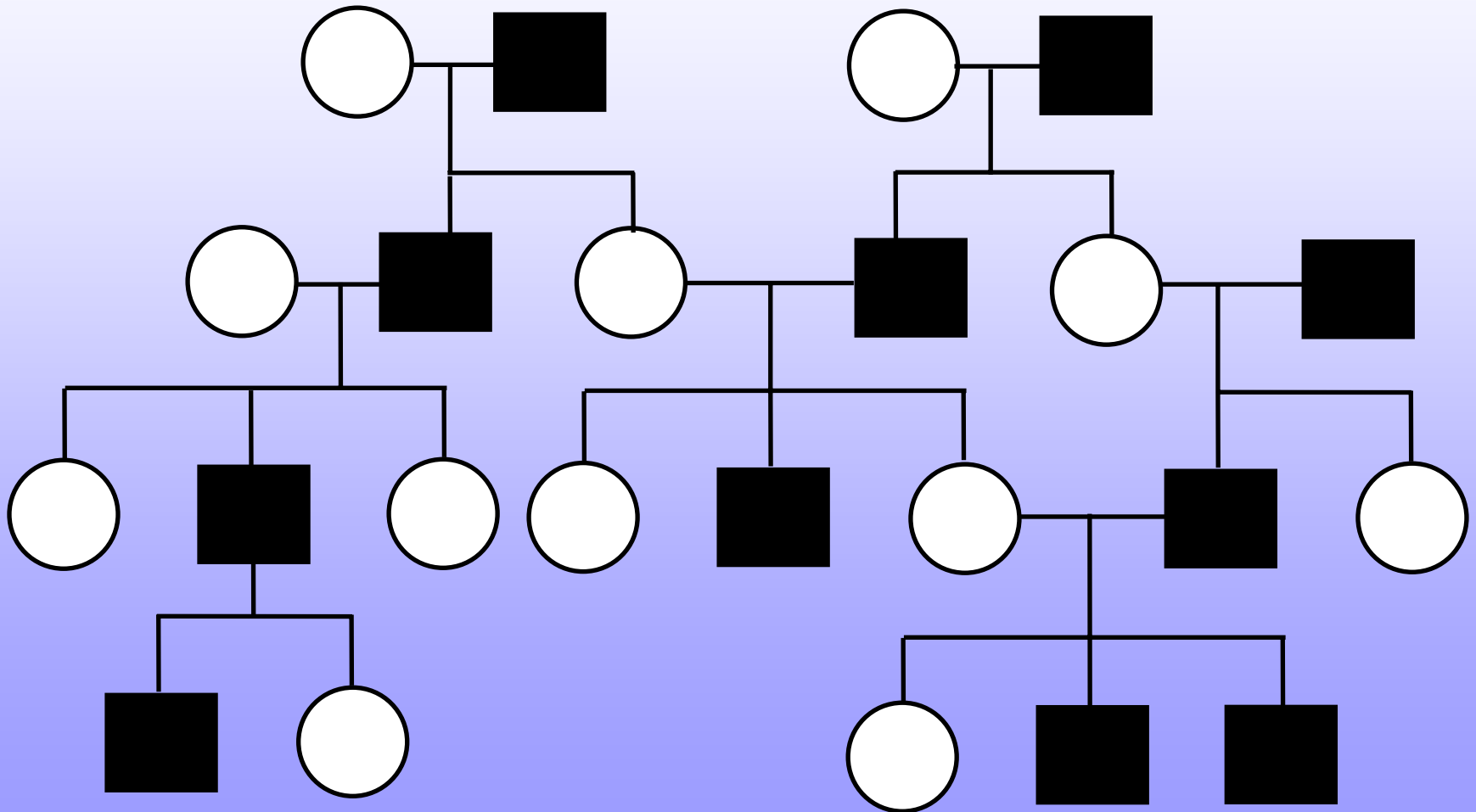
Lineage Markers

- Lineage markers are passed down from generation to generation without changing
 - Except for rare mutation events
- They can help determine the lineage (family tree) of an individual
- Y Chromosome Markers
 - Determine Paternal Lineage
- Mitochondrial Markers
 - Determine Maternal Lineage

Maternal Lineage



Paternal Lineage



Lineage Markers

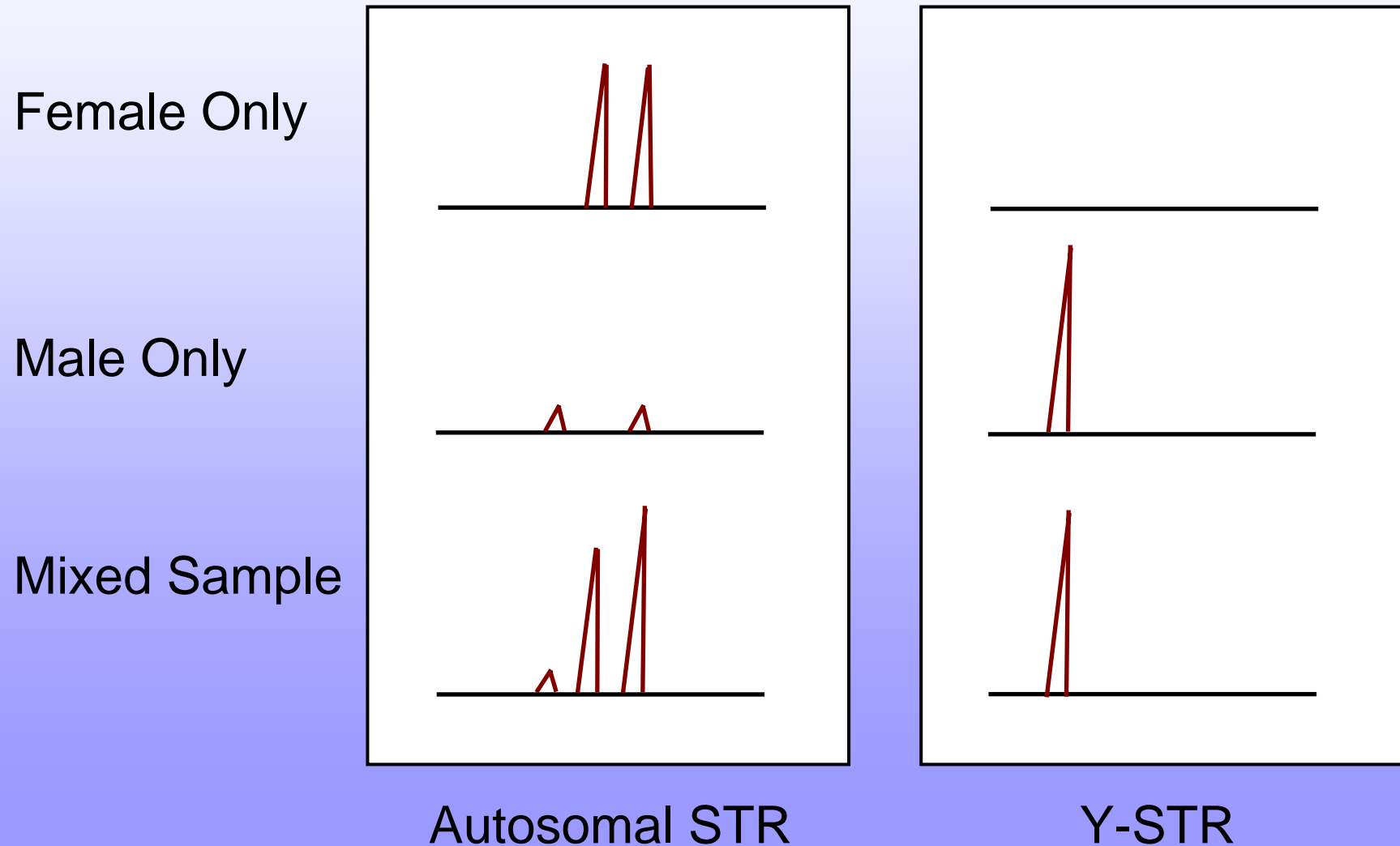
- Great for genealogy or tracing evolution
- However, the fact that these markers do not recombine is a disadvantage for Forensics
- Cannot use the product rule when determine the probability of an ID match
- Cannot separate direct relatives apart:
 - Y DNA Profile could be any male in family

Why Y Chromosome?

Markers on the Y Chromosome do have some advantages for Forensics:

- Sexual assault cases
- Absence of sperm may make it difficult to separate male DNA from female DNA
- May be overwhelming amount of female DNA – cannot read male genotype
- Identifying more than one male from single mixed sample

Female Male Mixed Sample



Reference Sample

Can use any male family member as a reference sample for Y-STR profile:

- Missing Persons
- Mass Disaster - ID'ing victims
- Paternity testing after suspected father has passed away or refuses to give sample for testing
- However you cannot tell male family members apart based solely on Y-STRs

Tracing Origins

Y-STRs are useful for tracing human origins through male lineage lines:

- Anthropological
- Historical
- Evolutionary history
 - Finding “Adam”
- Migration patterns
- Genealogical history

Y-STR Applications

Forensic Use	Advantage
Sexual Assault	Male specific amplification
Amelogenin Deficient Males	Analysis of Y-STRs proves male sample
Paternity Testing	If maternal sample is unavailable; only for sons
Missing Persons	Use any male relative as reference sample; only males
Human migration/evolution	Lack of recombination allows tracing lineage
Genealogical Research	Lack of recombination allows tracing lineage

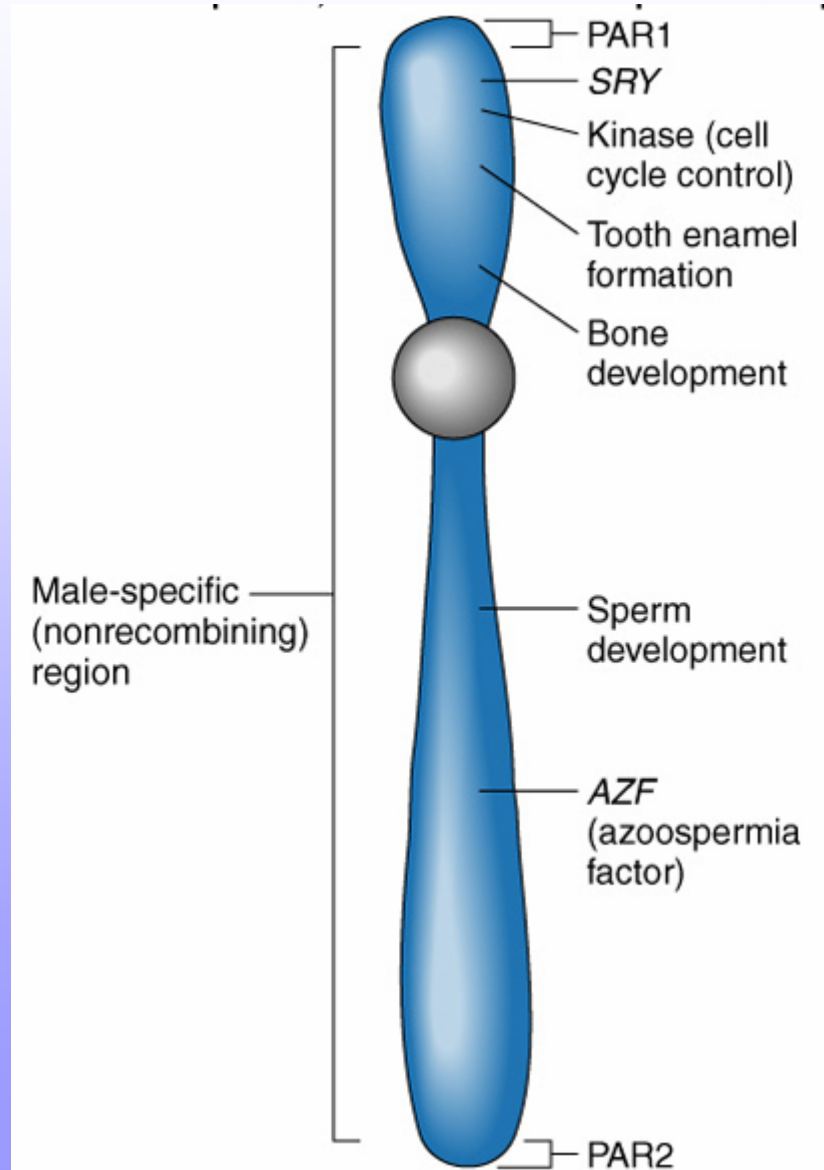
Y Chromosome

- Y chromosome has two parts:
 - Non-Recombining Portion – Y only
 - PAR – recombine with the X Chromosome
- Third smallest chromosome
- More than half of chromosome is heterochromatin – no genes
- Contains many repeats and palindromes
- For this reason primers sometimes may bind to more than one region of Y

Sex Chromosomes

- Y chromosome:
 - Contains ~90 genes
 - Majority of genes = Male Specific Region (MSR)
 - SRY gene – determines “maleness”
- X chromosome:
 - Contains ~1500 genes
 - Some dealing with sexual development
 - Most genes encoding proteins that have nothing to do with sex

Y Chromosome



Y-STRs

- Y chromosome contains same sort of variation as autosomes:
 - STRs
 - SNPs
 - Alu repeats
 - Minisatellites
- STRs give most information
 - More alleles per marker
 - High mutation rate

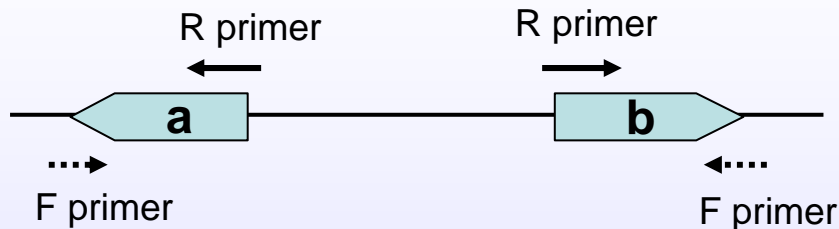
Minimal Haplotype

- 1997 a core set of Y-STRs were selected
- Population database has been set up with thousands of male haplotypes
- Core set:
 - DYS393
 - DYS391
 - DYS439
 - DYS438
 - DYS385a/b
 - DYS19
 - DYS437
 - DYS389I/II
 - DYS390
 - DYS392

Single Copy vs. Multi Copy

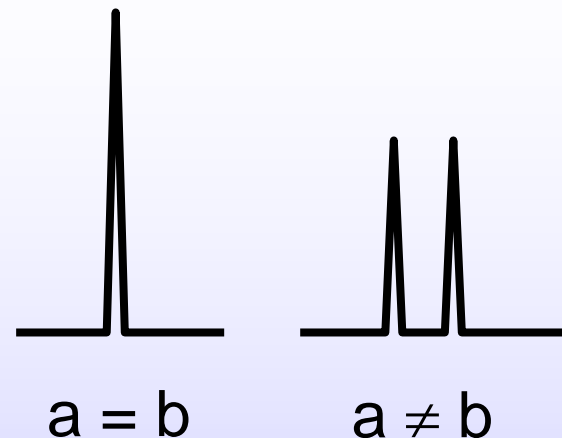
- Due to duplicated and palindromic regions on Y chromosome
- Some primers bind to multiple places
- Produce more than one PCR product
 - Multi Copy Markers
- DYS385 – produces two products
 - a and b
 - a and b can be either the same size or two different sizes

(A) DYS385 a/b

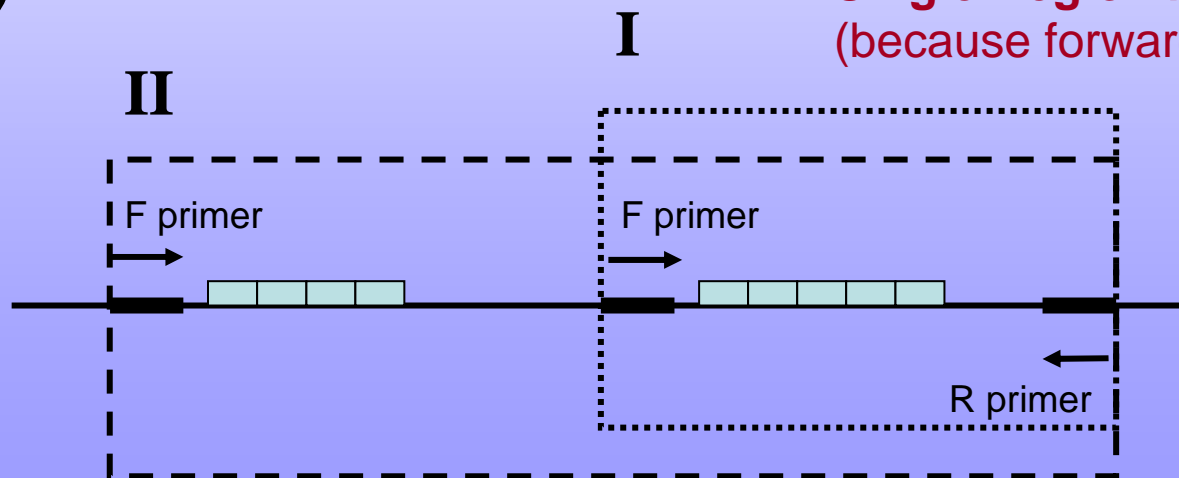


Duplicated regions are 40,775 bp apart and facing away from each other

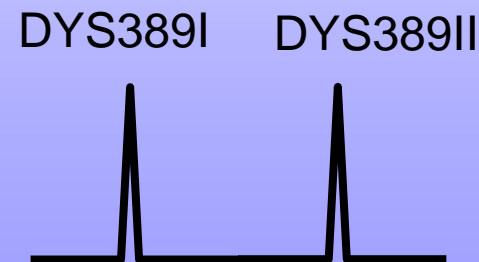
Multi-Copy (Duplicated) Marker



(B) DYS389 I/II



Single Region but Two PCR Products (because forward primers bind twice)



Multi Copy Y-STRs

- DYS385a/b
- DYS464a/b/c/d
- DYS389I/II
 - One primer, Forward, can bind to two places
 - 120 bp apart
 - This then makes two products using the same Reverse primer
 - One product is a subset of the other

Commercial Y-STR Kits

- Y-PLEX kit – minimal haplotype
- Some have 6 Y-STRs
- Others use 12 Y-STRs
- Some include the Amelogenin marker
 - Allow estimation of female: male ratio
- Advantage to having kits:
 - Every lab using same primers
 - Same allelic ladders

Commercial Y-STR Kits

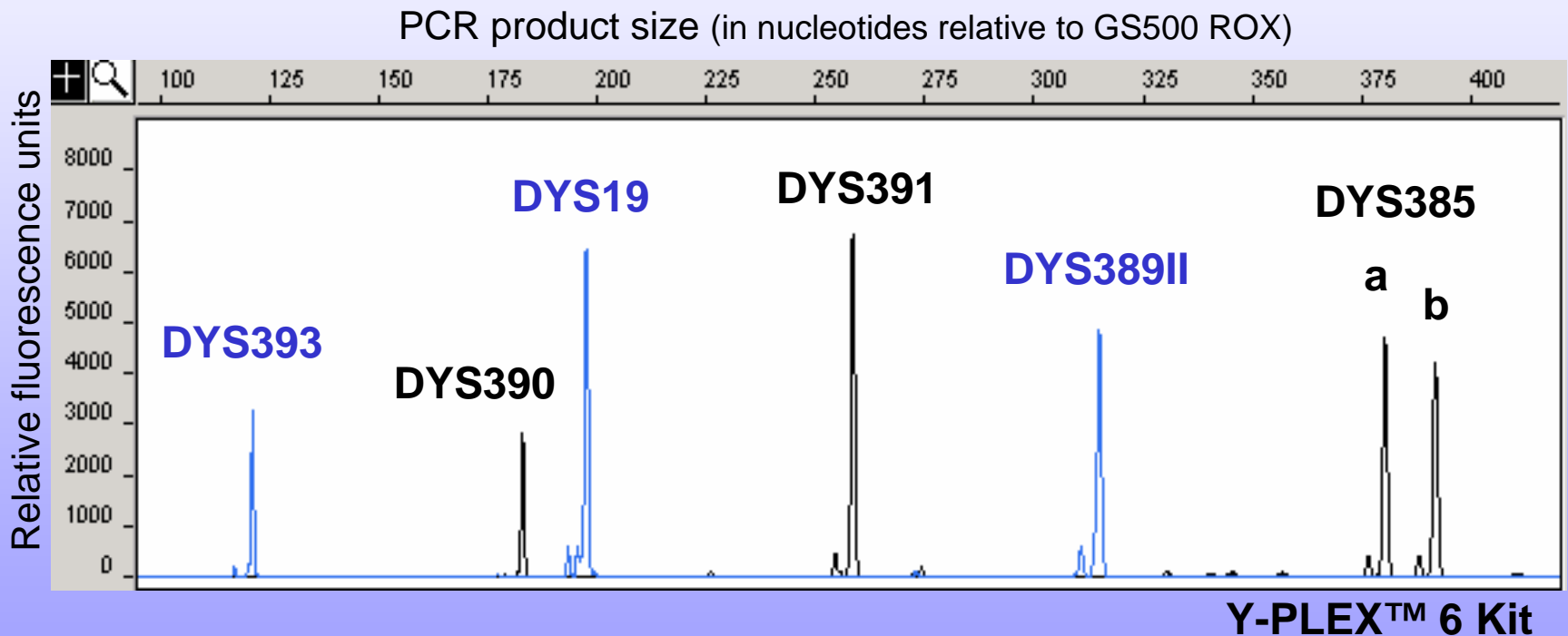


Figure 9.6, J.M. Butler (2005) *Forensic DNA Typing*, 2nd Edition © 2005 Elsevier Academic Press

Y-STR Haplotype Database

- www.ystr.org
- Minimal haplotype
- Typed on more than 25,000 individuals
- More than 36 different countries
- This allows population specific estimates of haplotype frequencies to be calculated for each Y-STR marker
- To determine how likely any given haplotype will be in any population

Interpreting Y-STR Profile

Three possible interpretations of Y-STR profile for Forensics:

1. Exclusion

- Cannot have originated from same sample

2. Inconclusive

- Insufficient distinguishing power to identify a match or not

3. Failure to exclude

- Sample may be from same source, or any male relative of source

Interpreting Y-STR Profile

Failure to exclude:

- Sample may be from same source, or any male relative of that source
- Cannot determine “Inclusion” like you can with autosomal STRs
- Why not?
- Y-STRs are useful for excluding a suspect, but not powerful enough to identify a unique “match”

Y Chromosome “Match”

- Means could be any male relative of suspect
- Interpretation should be qualitative rather than quantitative
- In court Y-STR profile must be presented very conservatively:
 - “The Y-STR profile from the crime scene matches to the suspect. Therefore we cannot exclude this suspect, any patrilineal relatives or an unknown number of unrelated males.”

Combining Y and Autosomal

- If results can be obtained from a limited number of Autosomal STR loci as well
- Then you will have added power to distinguish DNA sample
- Calculate most conservative minimum frequency for Y-STR profile
- Then multiply it by the frequency of whatever autosomal STRs you have
- Will calculate overall DNA Profile

Y-STR Allele Nomenclature

- Same rules as all STR's
- Same rules for the allelic ladders
- Name is based on core repeat unit:
 - Example – AGAT
- Also need to agree on where to start counting number of repeats:
 - First time repeat unit appears = 1
- Use first published report of marker

Positive Controls

- Within commercial kits – also get 5 male DNA samples
- Use as positive controls
- Make sure all genotyping is consistent across laboratories
- Autosomal STRs also come with positive controls
 - CEPH families

Mutation Rates

- Mutation rates calculated for Y-STRs
- In same range as autosomal STRs:
 - 1-4 per 1 thousand meioses
- Important note – must remove illegitimacy
 - Sometimes people are wrong about paternity
- Not easy to separate mutation events from illegitimate paternity
 - Unless you also have autosomal STRs

Mutation Events

- Mutation events interfere with:
 - Paternity analysis
 - Mixture interpretation
- Especially when mutational event is duplication or triplication or a locus
- Recommendation: Differences at three or more Y-STR loci are needed before exclusion can be determined
 - Actually same rule for autosomal STRs

Real Life Use of Y-STRs

- New York City Office of Chief Medical Examiner
- Uses Y-STR in any of the following conditions:
 - Evidence is positive for semen but no male DNA is found in genotypes
 - Male/Female mixture is known to exist
 - Large number of semen stains need to be separated and ID'd
 - Evidence of more than one male perpetrator

Bi-Allelic Markers

- Y Chromosome also has:
 - SNPs
 - Alu repeats
- Since these markers have lower mutation they are more useful for ancestral and genealogy studies
- Compare human Y DNA to Chimp Y DNA to determine “ancestral allele”

Historical Questions

- Evolutionary tree
 - Try to determine how humans evolved from ancestors by following lineage markers
- Human migration patterns
 - Determine the path that brought humans from Africa to Asia and Europe
- Differences between races
 - Compare African-American's haplotypes vs. European Caucasian's haplotypes

Genealogical Studies

- Genghis Khan
 - Men in Asia traced to Genghis Khan's Y chromosome
- Family History
 - Trace your own genealogy
- Surname testing
 - Since Surname (Last Name) follows the father's lineage in most cultures
 - Common origin of the Surname traced by Y chromosome testing

Future of Y Chromosome Testing

- Commercial kits make Y-STRs more available and more compatible between laboratories
- Additional markers are being tested
- New population studies are being done
- More accurate likelihoods of Y-STR profiles can be calculated
- Both lineage analysis and Forensics can use Y chromosome markers

Any Questions?

Skip over Jefferson/Hemmings story

Read Chapter 10

Likelihood of Y-STR Profile

Three mathematical approaches are used to calculate the likelihood of seeing a Y-STR profile

1. Counting method

- $p = X(\# \text{ this exact profile})/N$ (# total profiles)

2. Bayesian approach

- Calculates plausibility of any match

3. “Mismatch” distribution

- How often a random sample matches

SRY Gene

- **SRY** = **S**ex-determining **R**egion of **Y**
- A transcription factor (TF)
 - TF's are genes that control the expression of other genes (turn on/off)
- SRY turns on “male” genes
- “Male” genes activate male hormones
- Male hormones (testosterone) end up producing male structures
- Also, destroy female structures

Questions

- What advantages does genotyping Y-STRs have over autosomal STRs?
- What disadvantages?
- How will the increase in availability of Y-STRs kits make a difference?
- How do you determine the frequency of a Y-STR DNA profile?
- Why is it more complex than autosomal STRs?