LEIDEN UNIVERSITY MEDICAL CENTER

Y-STRs and population sampling for forensic reference purposes

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Introduction

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- A small number of these loci can already be used for identification.
  - Only 13 are used in the US.
  - Each STR allele is common in 5% to 20% of a population.
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  - Only 13 are used in the US.
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  - Chance of a false positive: $1 \cdot 10^{-18}$ (rough estimate).
    - However, a false positive match was found in 2007, in a database of 30,000 samples.
    - There are also about $12 \cdot 10^{6}$ monozygotic twins.

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Determination by sequencing (J.W.F. van der Heijden, K.J. van der Gaag, P. de Knijff, J.F.J. Laros) :

- After amplification, sequence the amplicons.
- With *semi-global alignment*, determine the exact repeat pattern.
    - The length can be determined on the nucleotide level.
    - Diversity within the repeat can be identified.

Estimation of diversity

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An underestimation of the frequency of commonly shared Y-STR haplotypes can be unfavourable for a suspect.

The Rucphen study

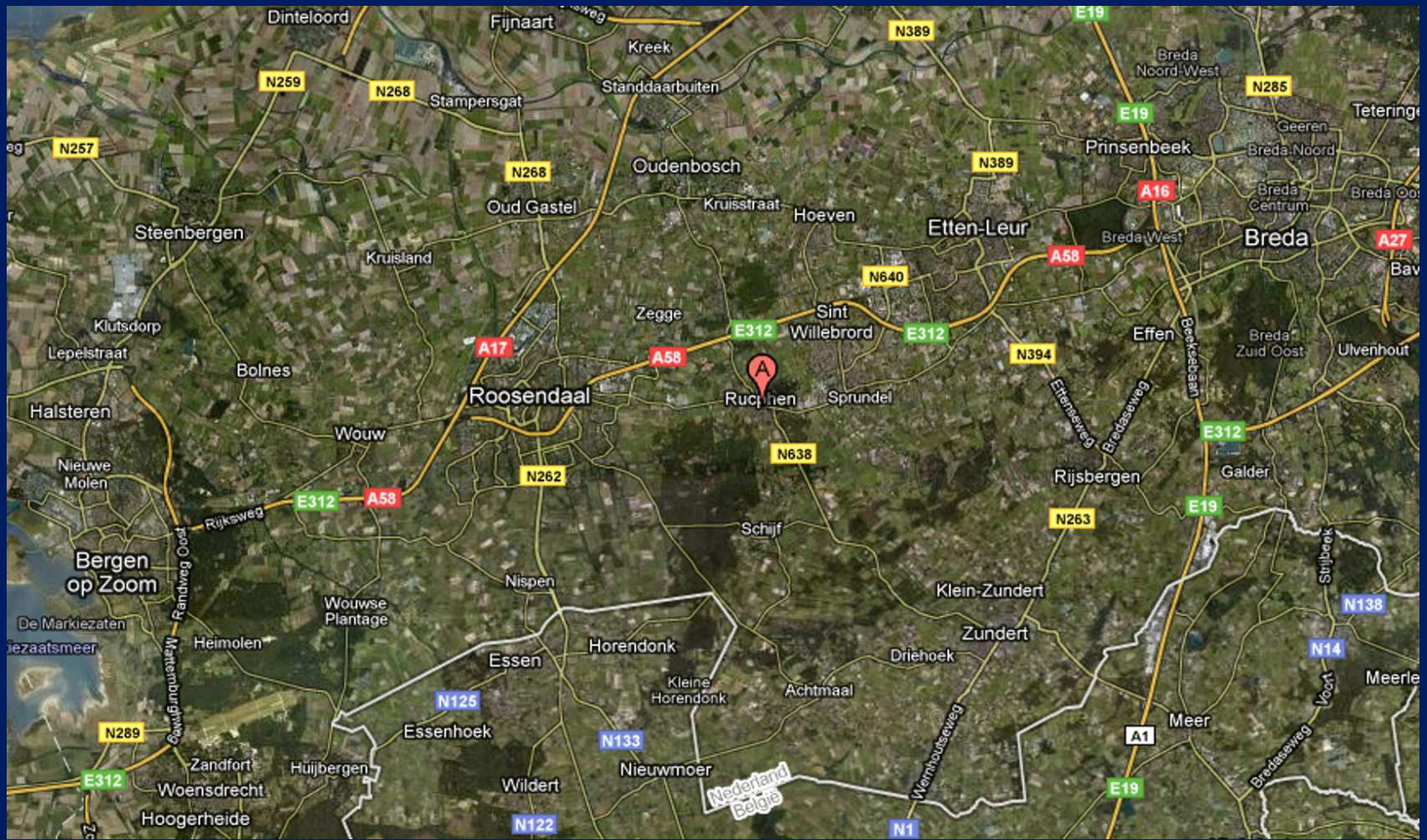

Figure 1: Rucphen, Noord-Brabant.

The Rucphen study

Set up:

- Random selection of 1350 males from Rucphen.
- Genotype for 15 autosomal STR loci, 25 Y-SNPs, 12 Y-STR loci.
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- Select 100 random subsets of 100 males using different criteria:
  - Fully random.
  - Fully unrelated.
  - Random, not allowing 1 generation differences.
  - Random, not allowing 1 or 2 generation differences.
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- Calculate *haplotype diversity* for Y-STRs.
- Calculate *probability of identity* for autosomal STRs.

Paternal family trees

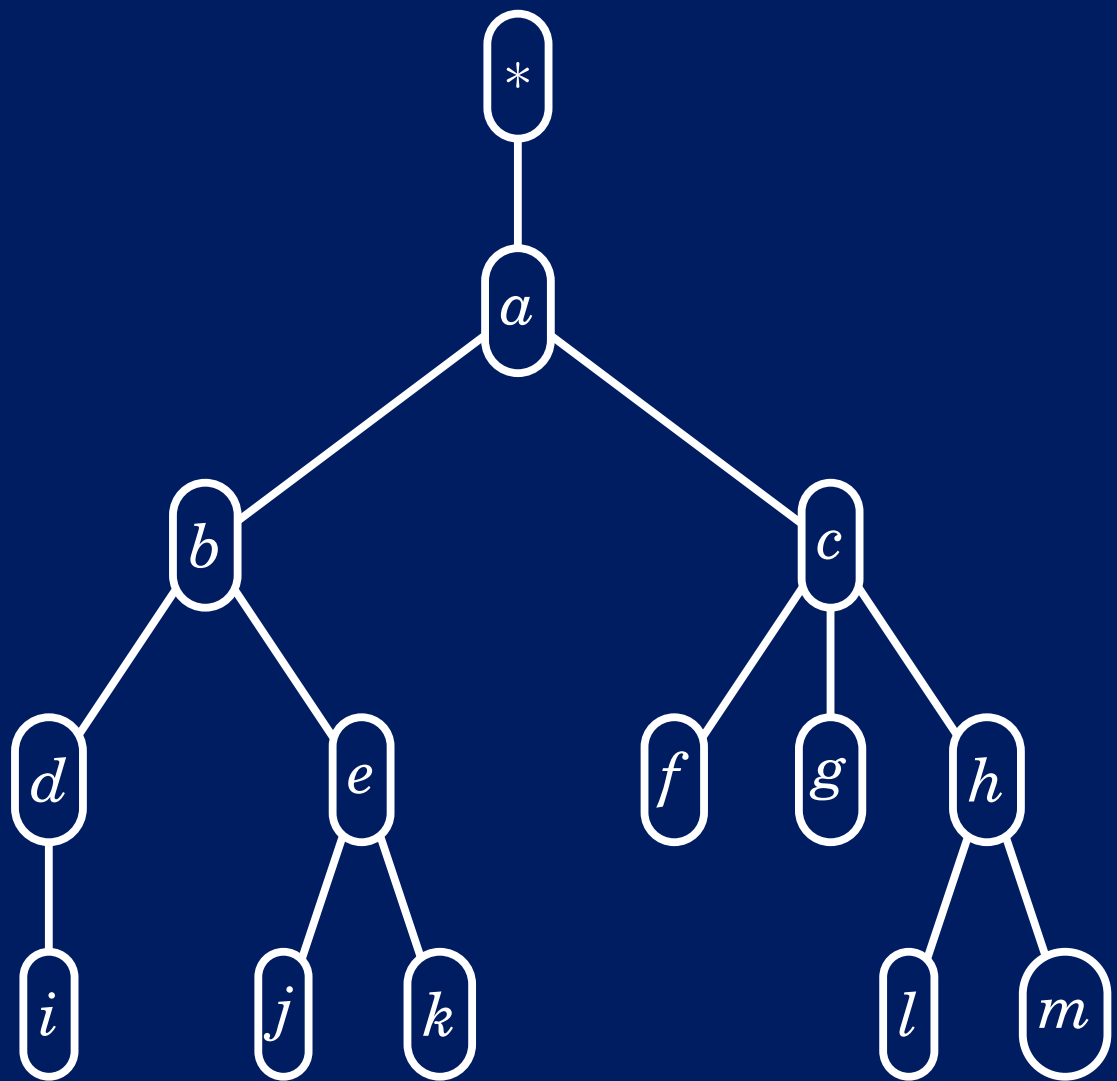
A *linkage pedigree data* (PED) file consists of the parents of a person on each line.

Family id, Person id, Paternal id, Maternal id, Sample id.

0,	1,	0,	0,	1
0,	2,	1,	0,	2
0,	3,	1,	0,	3
0,	4,	2,	0,	4
0,	5,	2,	0,	5
0,	6,	3,	0,	6
0,	7,	3,	0,	7
0,	8,	3,	0,	8
0,	9,	4,	0,	9
0,	10,	5,	0,	10
0,	11,	5,	0,	11
0,	12,	8,	0,	12
0,	13,	8,	0,	13

Table 1: An example PED file.

Paternal family trees



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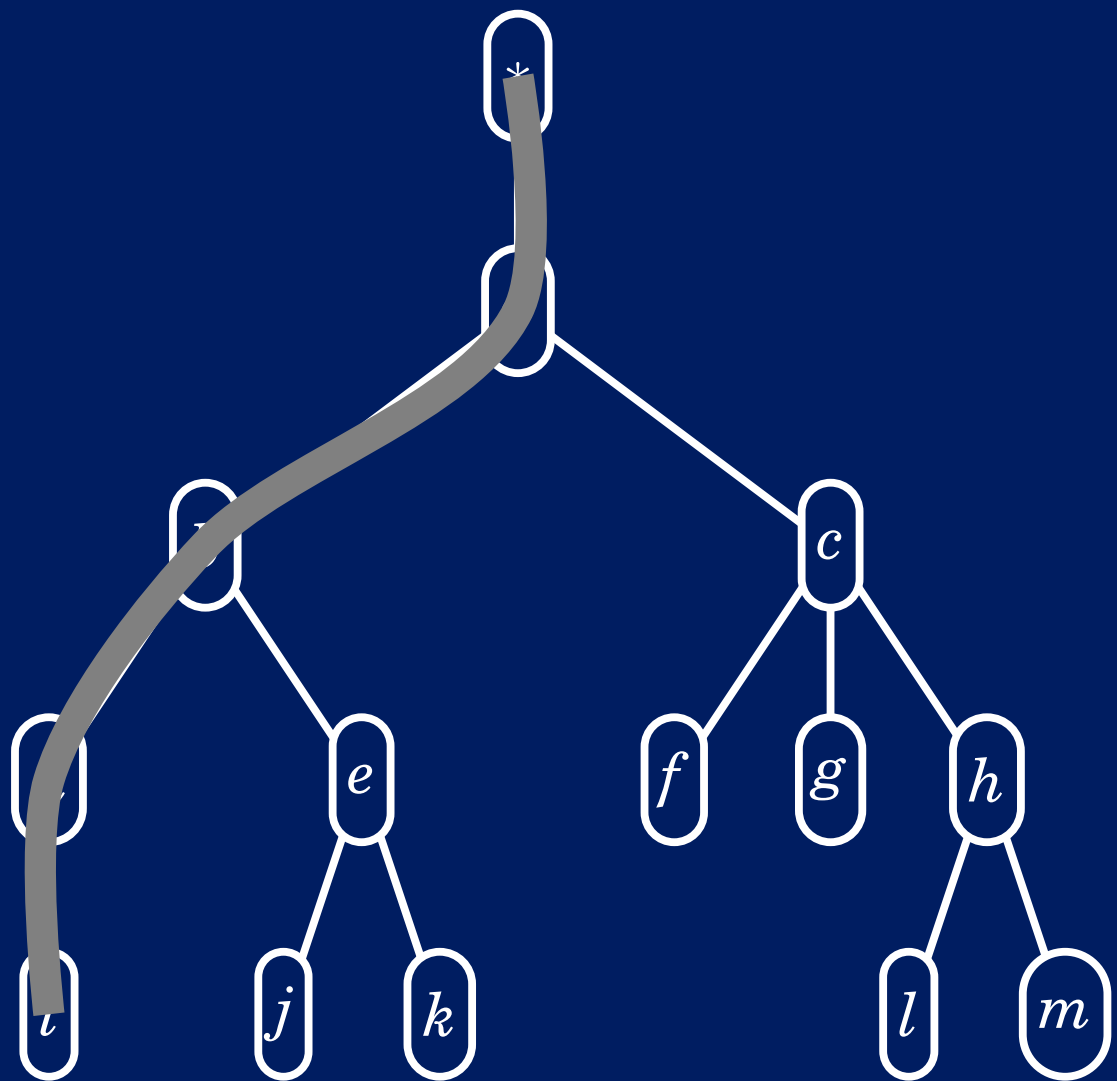

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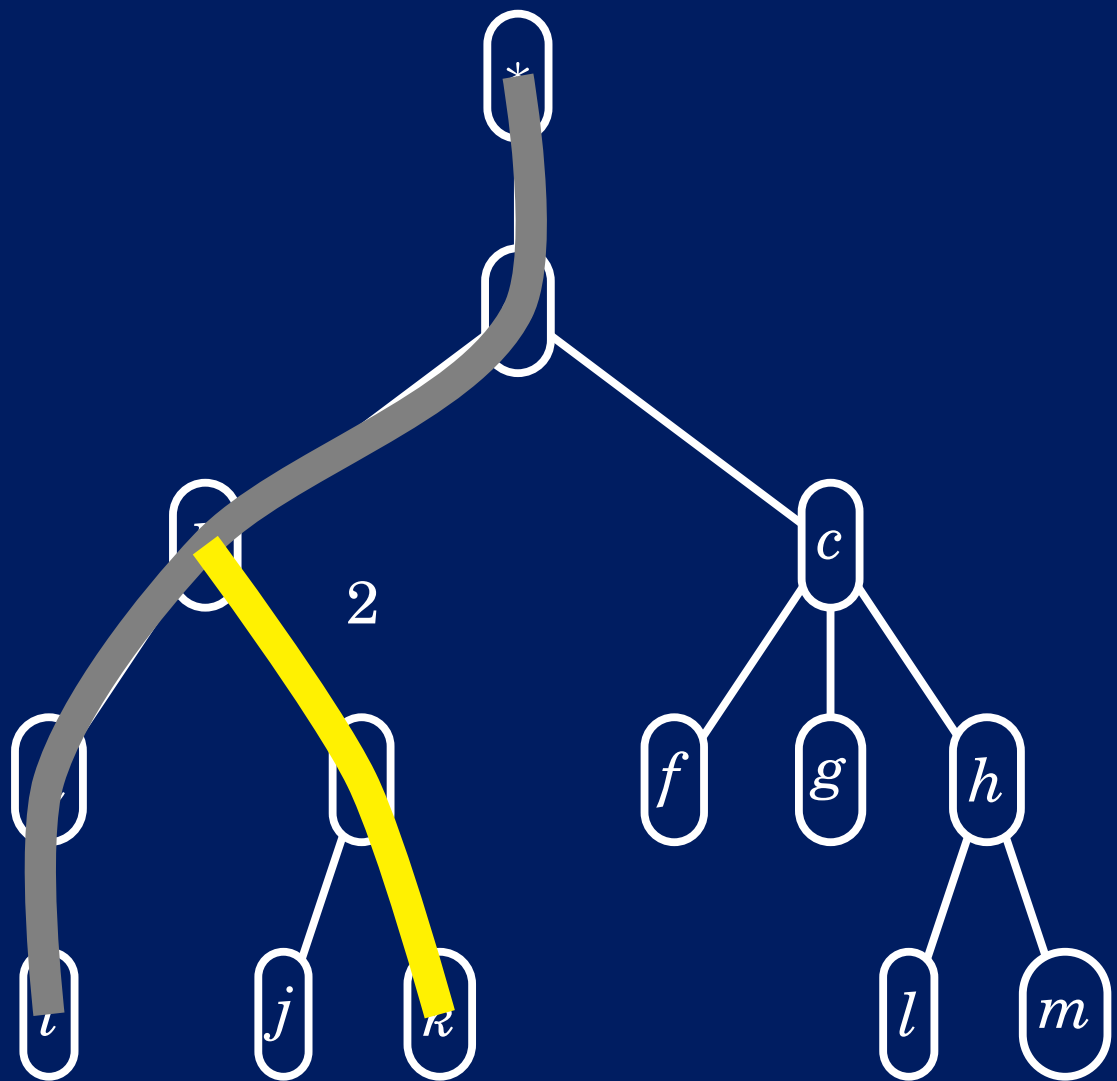

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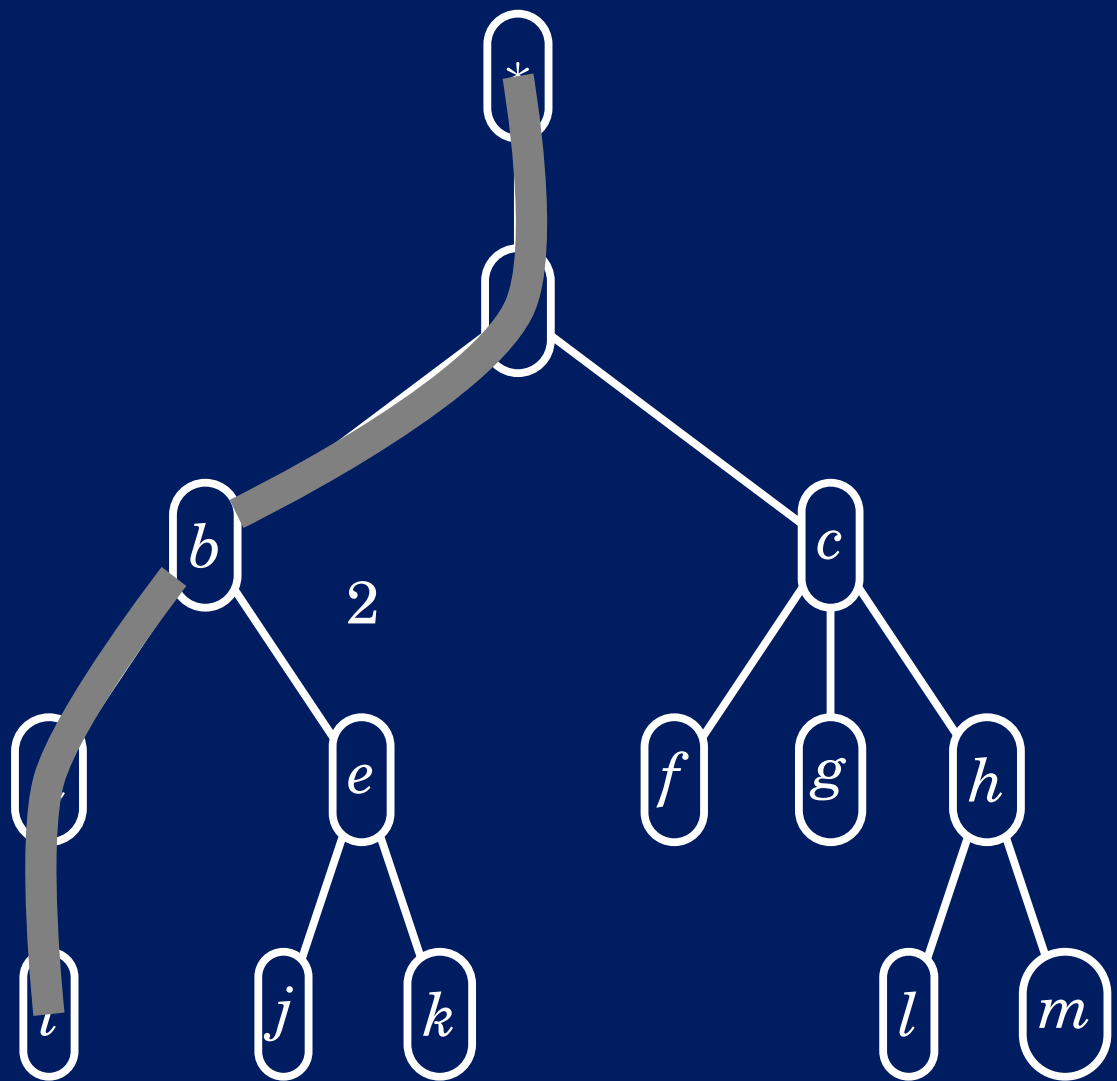

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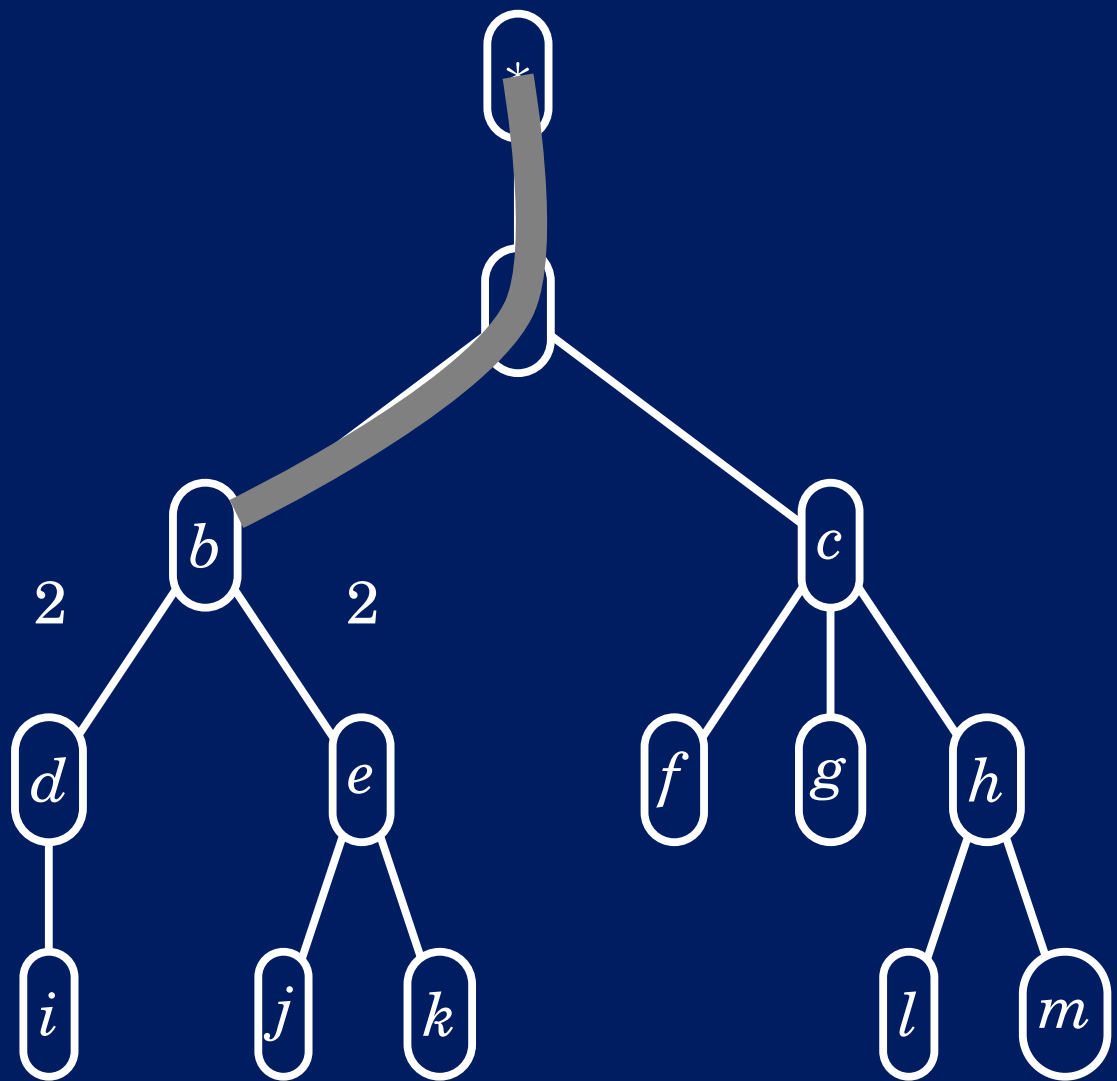

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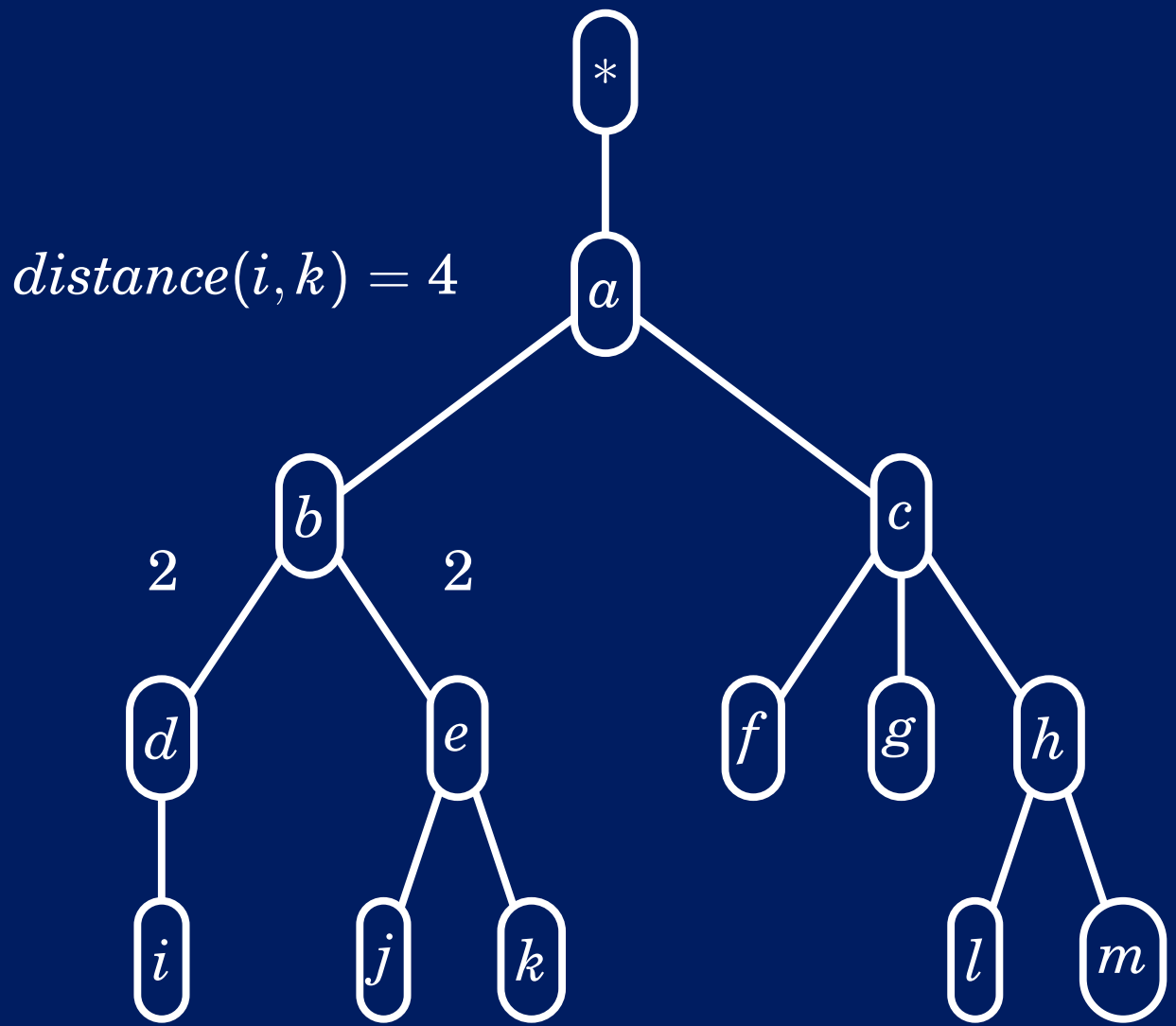

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Implementation note:

A node is represented by an object which has various attributes.

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- A flag to mark a visited node.
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This dual data structure allows us to quickly access any node in the tree and determine the path to the root of the tree easily.

Paternal family trees

dist(x,y)	a	b	c	d	e	f	g	h	i	j	k	l	m
a	0	1	1	2	2	2	2	2	3	3	3	3	3
b	1	0	2	1	1	3	3	3	2	2	2	4	4
c	1	2	0	3	3	1	1	1	4	4	4	2	2
d	2	1	3	0	2	4	4	4	1	3	3	5	5
e	2	1	3	2	0	4	4	4	3	1	1	5	5
f	2	3	1	4	4	0	2	2	5	5	5	3	3
g	2	3	1	4	4	2	0	2	5	5	5	3	3
h	2	3	1	4	4	2	2	0	5	5	5	1	1
i	3	2	4	1	3	5	5	5	0	4	4	6	6
j	3	2	4	3	1	5	5	5	4	0	2	6	6
k	3	2	4	3	1	5	5	5	4	2	0	6	6
l	3	4	2	5	5	3	3	1	6	6	6	0	2
m	3	4	2	5	5	3	3	1	6	6	6	2	0

Table 2: Distance of all persons in the tree of Figure 4.

More than one family in the same tree

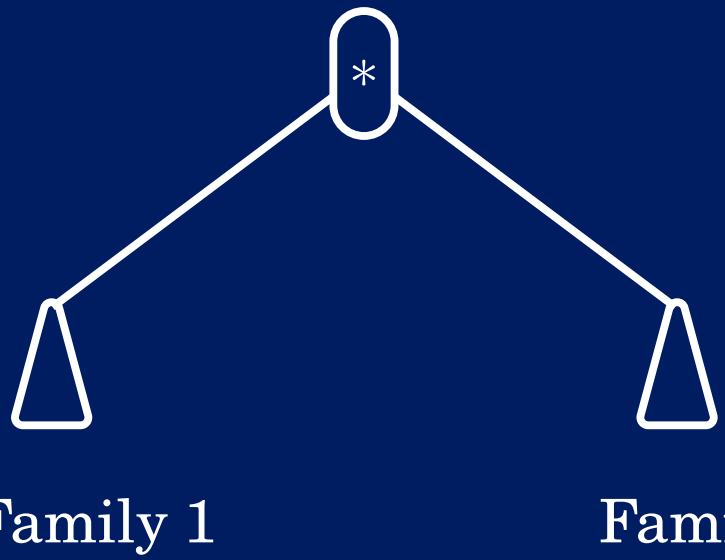
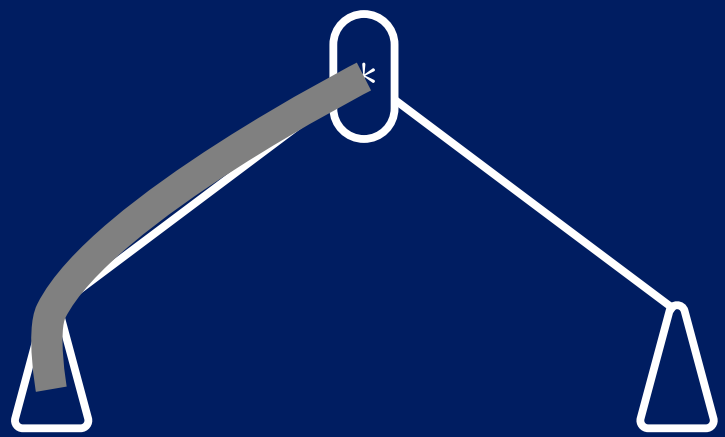


Figure 3: Combining families in one tree.

When we encounter the $*$ node with the yellow line, we know people are unrelated.

More than one family in the same tree



Family 1 Family 2

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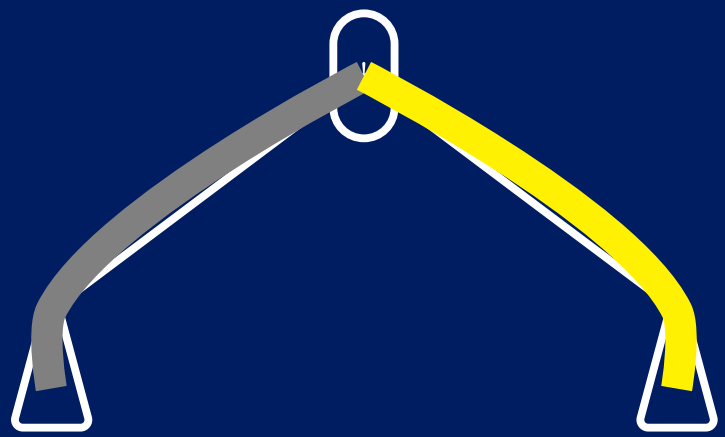

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Note that this is not very efficient, but trivial to implement.

Relatedness in our selection

The resulting 1328×1328 matrix gives the relatedness of each pair of persons in our selection.

Generations	Count	Generations	Count
1	343	13	409
2	376	14	98
3	440	15	70
4	591	16	42
5	562	17	21
6	824	18	184
7	905	19	438
8	822	20	370
9	916	21	116
10	1100	22	12
11	1131	23..99	0
12	852	100	870506

Table 3: Summary generations matrix.

Note that we use 100 to indicate unrelatedness.

Selecting people on relatedness

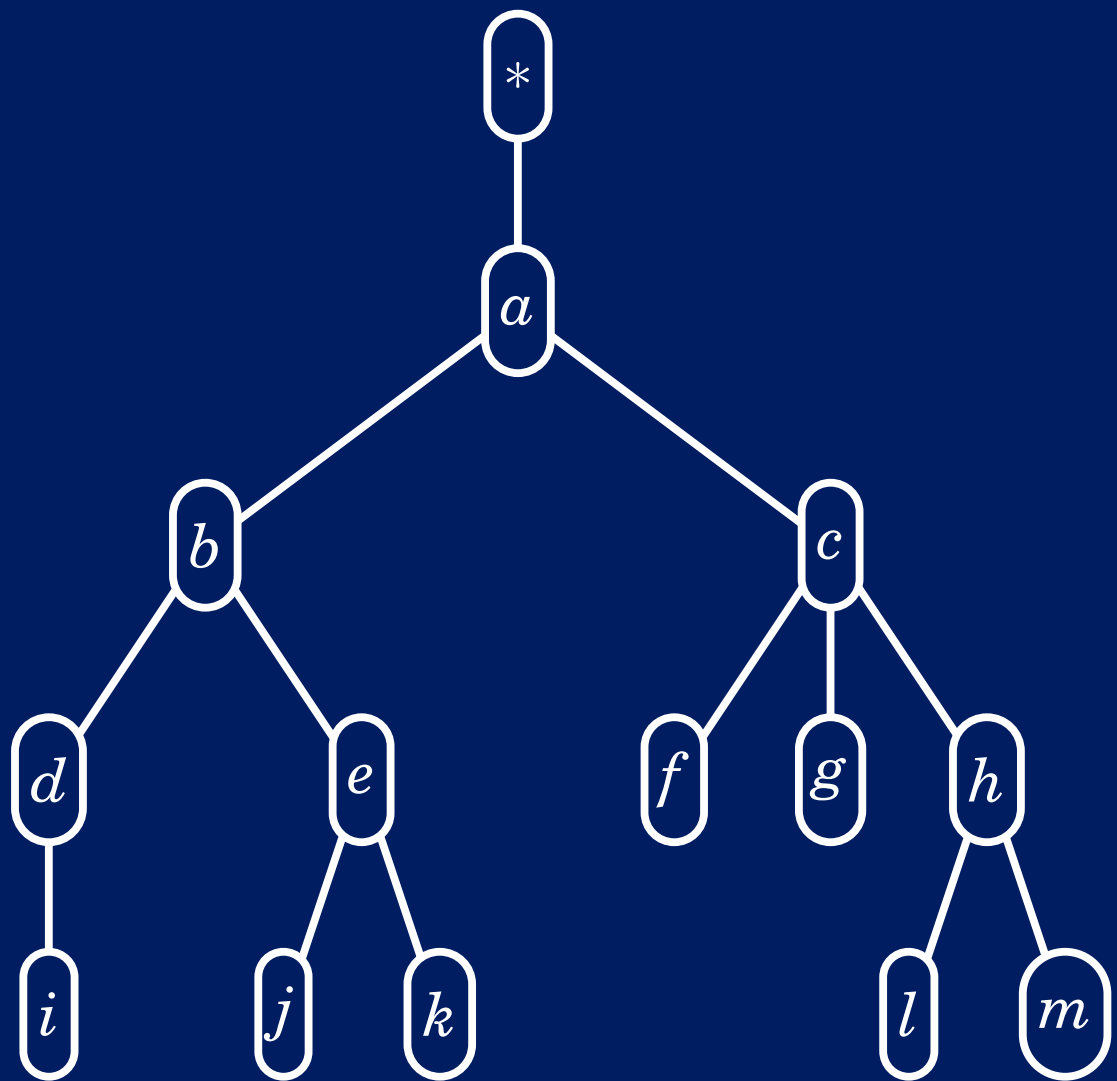
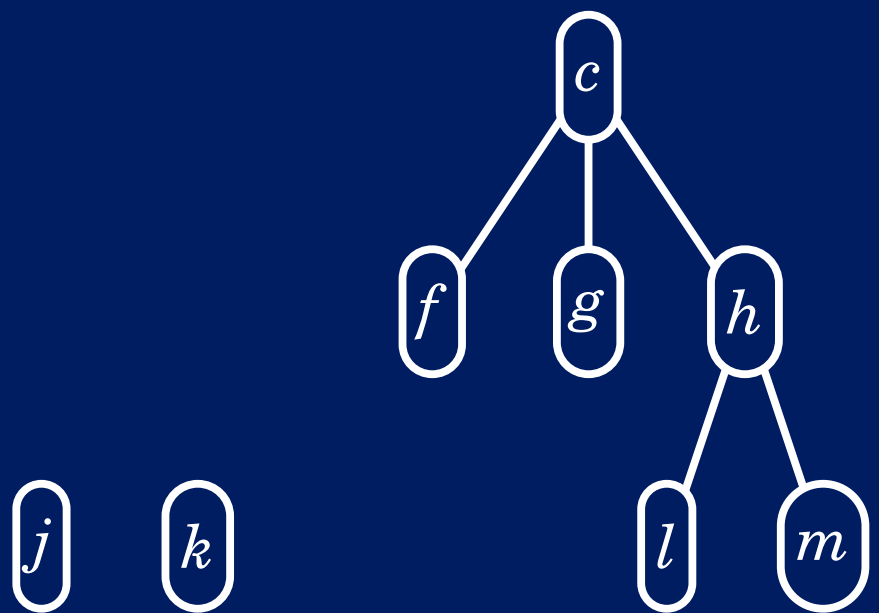


Figure 4: Paternal family tree of Table 1.

Selecting people on relatedness

Person i and everyone within distance 3 removed.



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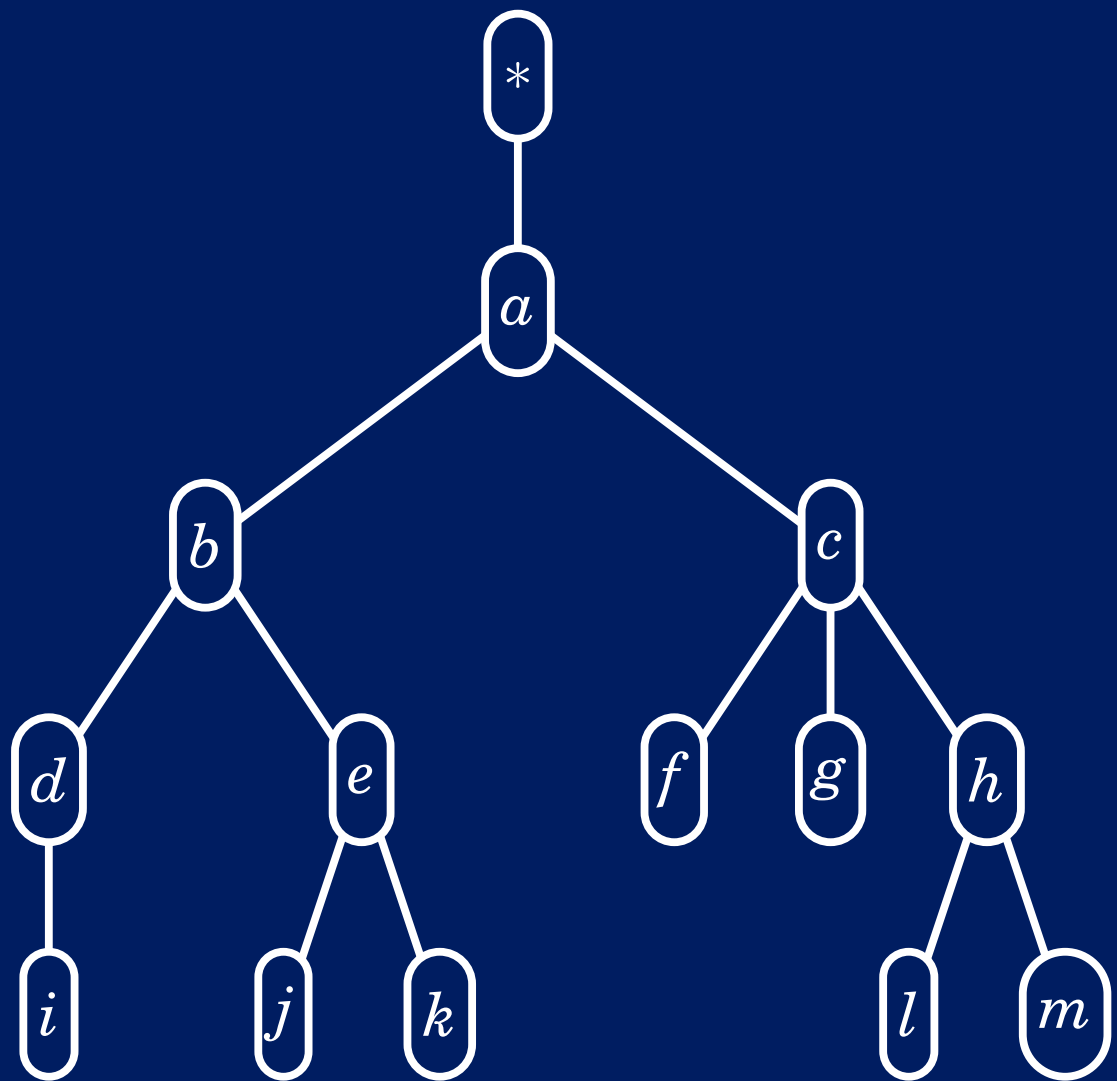

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Selecting people on relatedness

We make a list of persons that are within a certain distance.

Person	Family			
a	b	c		
b	a	d	e	
c	a	f	g	h
d	b	i		
e	b	j	k	
f	c			
g	c			
h	c	l	m	
i	d			
j	e			
k	e			
l	h			
m	h			

Table 4: Family members within distance 1.

This can easily be extracted from the distance matrix.

Selecting people on relatedness

We make a list of persons that are within a certain distance.

Person	Family			
c	a	f	g	h
f	c			
g	c			
h	c	l	m	
i	d			
j	e			
k	e			
l	h			
m	h			

Table 5: Table 4 after selecting person b.

Removed persons can still have a reference.

Results

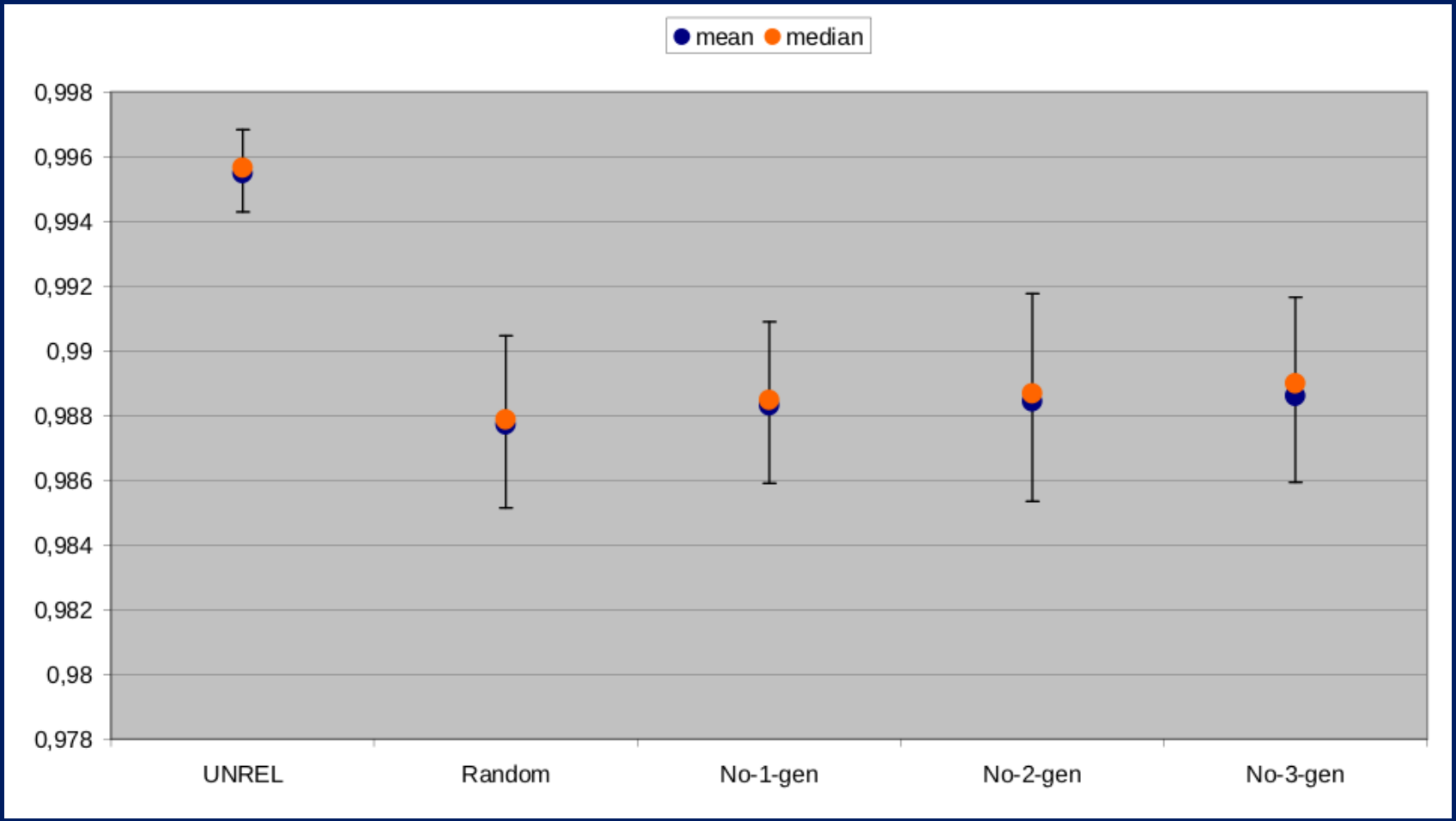

Figure 5: Chromosome-Y haplotype diversity.

Results

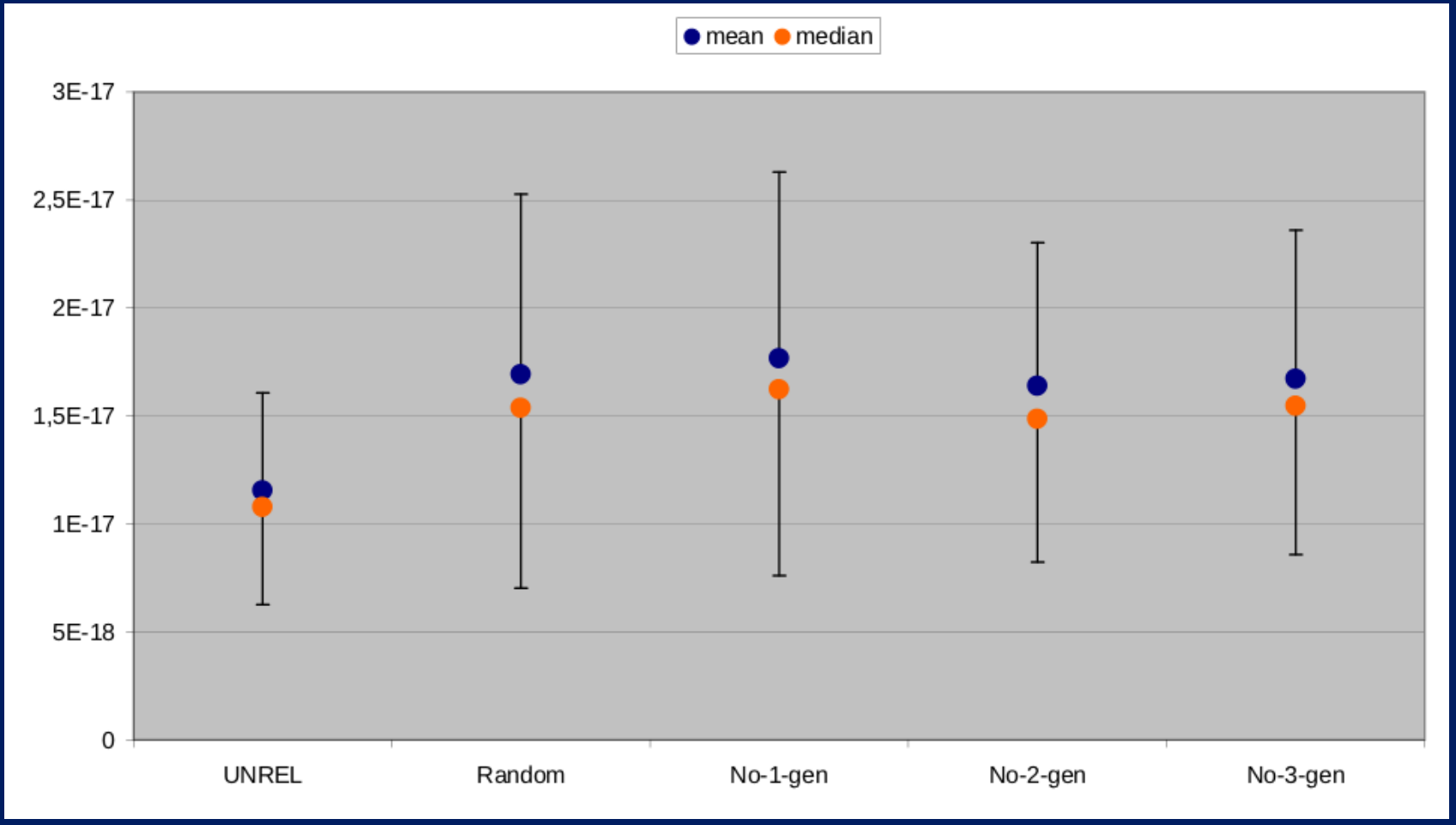

Figure 6: Probability of identity (autosomal STRs only).

Conclusions and further research

We have empirically proven the following:

- Drawing a random sample from a population using the classical selection rule does not result in a truly random subset.
    - This has little effect when using autosomal STR markers.
    - The effect is significant when using Y-STR markers.

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Questions:

- Are the most abundant haplotype frequencies underestimated?

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Acknowledgements:

Thirsa Kraayenbrink
Manfred Kayser
Peter de Knijff

https://www.mutalyzer.nl/svn/generations/