Y Chromosomal STR Markers: Assessing Evidential Value

FOSW03: Statistical Modelling of Scientific Evidence

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... and many others!

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Outline

- The discrete Laplace model (quick*ish* recap)
- Comparing match probability estimators
- Population substructure

Motivation

of the discrete Laplace model

Statistical model

$$P(h) \geq 0 \quad \text{and} \quad \sum_{h \in \mathcal{H}} P(h) = 1$$

(Forensic genetic) applications:

- $LR = \frac{P(E|H_p)}{P(E|H_d)}$
- $P(h)$
- $\theta + (1 - \theta)P(h)$
- Mixture deconvolution
- *LR* for mixtures (qualitative/quantitative)
- Cluster analysis (not shown)
- Not a new ad-hoc tool for each task

Model

- Y-STR: Loci not statistically independent
- Our approach: Condition on [something] to obtain independence between loci

The Discrete Laplace model

for Y-STR haplotypes (MM Andersen *et al.*, 2013)

$$f(x; p, \mu) = \frac{1-p}{1+p} \cdot p^{|x-\mu|} \quad \text{for } x \in \mathbb{Z},$$

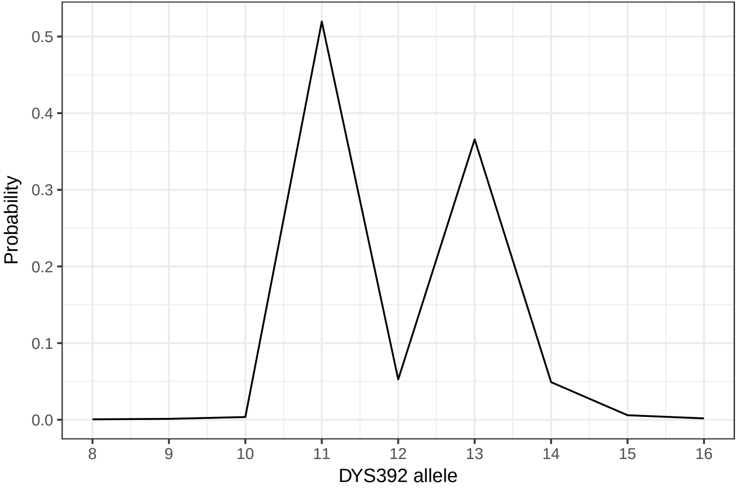
$$P(X = \vec{x} = (x_1, x_2, \ldots, x_r)) = \sum_{j=1}^{c} \tau_j g\left(\vec{x}; \vec{p_j}, \vec{\mu_j}\right) = \sum_{j=1}^{c} \tau_j \prod_{k=1}^{r} f\left(x_k; p_{jk}, \mu_{jk}\right),$$

$$p_{jk} = \exp\left(\alpha_j + \beta_k\right).$$

- Estimation: EM algorithm w/ GLM heavily exploiting structure of design matrix
- Parameter estimation from observations using `R` library `disclapmix`

Data and fit

1,692 Germans from Purps (2014) Y23



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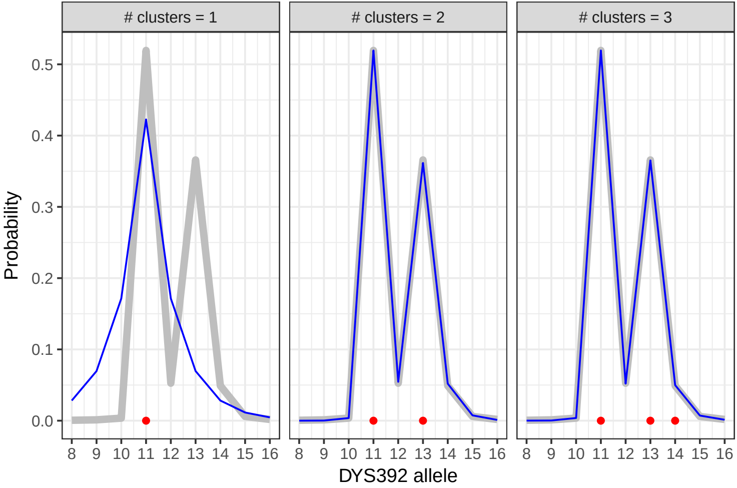

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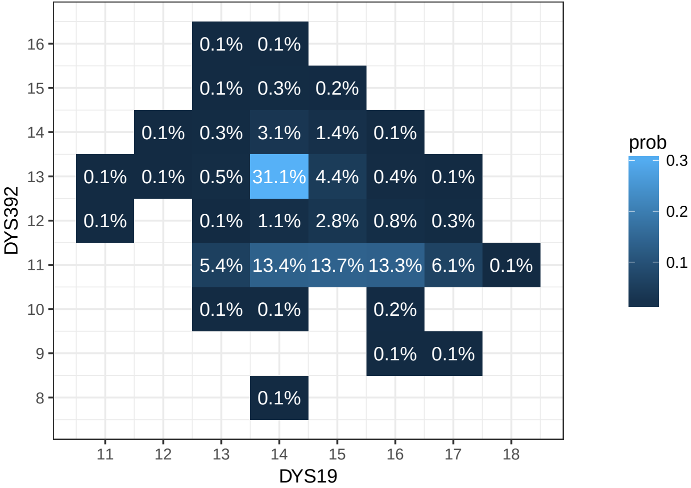

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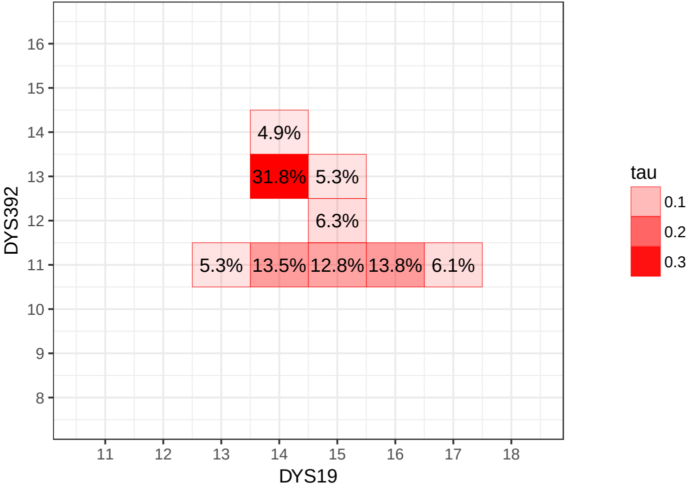

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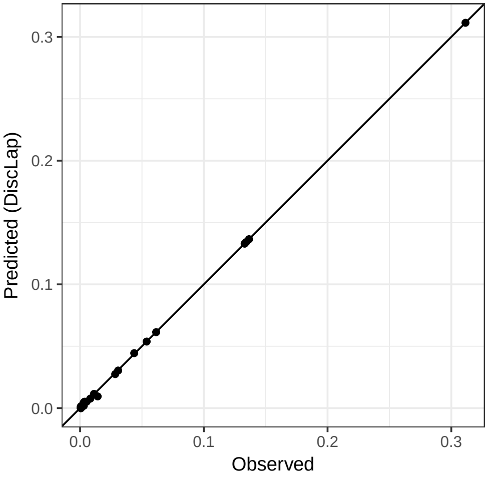

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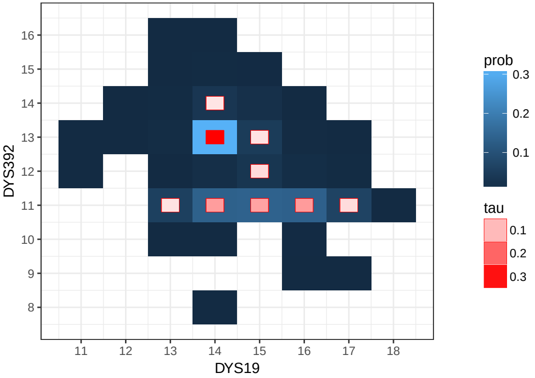


- $(\text{rows} - 1)(\text{columns} - 1) = (9 - 1)(8 - 1) = 8 \cdot 7 = 56$
- $(r \cdot c) + (c - 1) + (r + c - 1) = (2 \cdot 9) + 8 + (2 + 8) = 36$
  - $p_{jk} = \exp(\alpha_j + \beta_k)$, $\beta_1 = 0$

Estimator validation

Estimator validation

- Single source stain
- No errors
- No peak heights
- Compare/validate/investigate estimators estimating different population quantities
  - Data reduction

LR and donorship

- Case
  - Profile from donor to crime scene stain, h_{donor}
  - Profile from suspect, h_{suspect}
  - Reference database
- Decision problem: Is the suspect the donor? Tried solved by *LR*
  - Simple case: $LR = 1/\text{match probability} = 1/\text{population frequency}$
- Higher *LR*, more evidence that the suspect is the donor
- Trade-off: Conservative (when possible) vs informative
  - Data reduction
  - Non-match $\Rightarrow LR = 0$ and match $\Rightarrow LR = 1$

Simulate cases

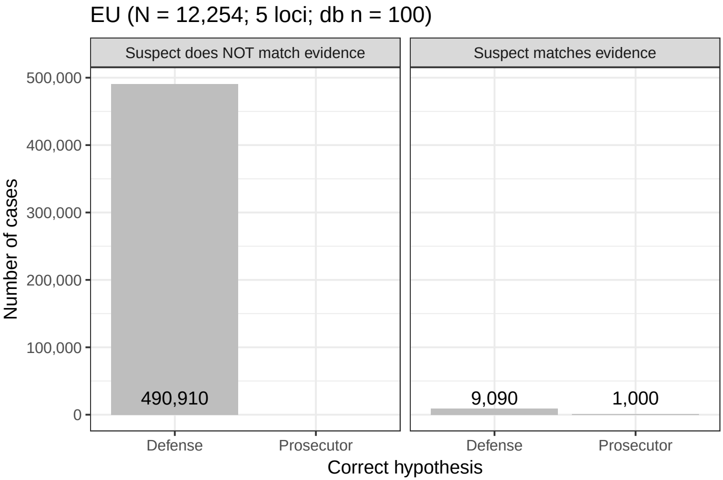
Population:

- EU on 5 loci from Purps (2014) Y23 dataset ($N = 12{,}254$)
  - 2.9% of haplotypes are singletons

Cases:

- Simulate cases under H_p (suspect is the donor), $k_p = 1{,}000$
  - Simulate reference database ($n = 100$)
  - Simulate the suspect's/donor's haplotype
- Simulate cases under H_d (suspect is not the donor), $k_d = 500{,}000$
  - Simulate reference database ($n = 100$)
  - Simulate the suspect's haplotype, h_{suspect}
  - Simulate the donor's haplotype, h_{donor}
  - Often, $h_{\text{suspect}} \neq h_{\text{donor}} \Rightarrow LR = 0$

Simulate cases



Estimators

Database size n:

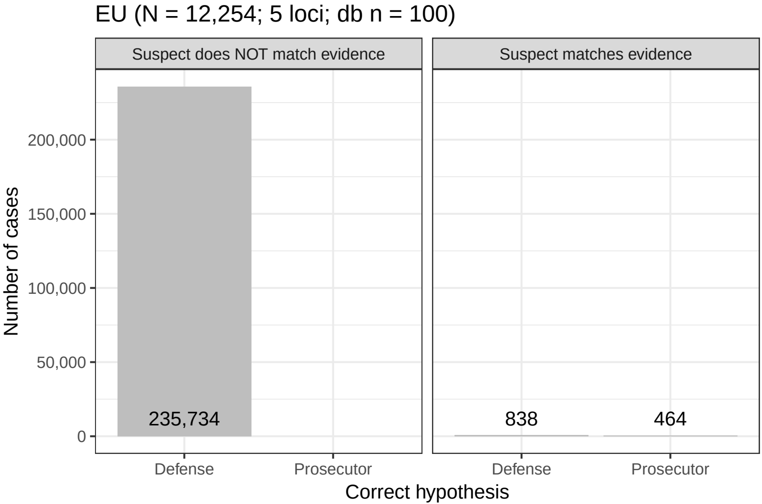
- n_1 = # singletons
- n_2 = # doubletons
- $\kappa = n_1/n$

Estimators:

- Kappa (CH Brenner): $LR_{\text{rare}} = n/(1-\kappa) = n \cdot \frac{n}{n-n_1} > n$
- Generalised Good (G Cereda): $LR_{\text{rare}} = (n \cdot n_1)/(2 \cdot n_2) = n \cdot \frac{n_1}{2n_2}$ also LR for non-rare
- Discrete Laplace (MM Andersen)
- (~~Coalescent: Not included due to computational requirements, could be interesting~~)
- (~~Chinese restaurant (G Cereda): Work on including it is in progress~~)

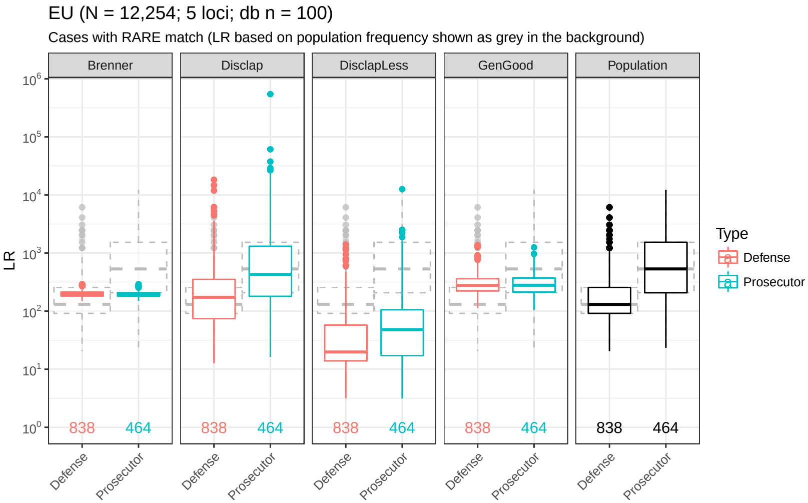
Cases

Rare/unobserved haplotypes



LR distribution

Rare/unobserved haplotypes

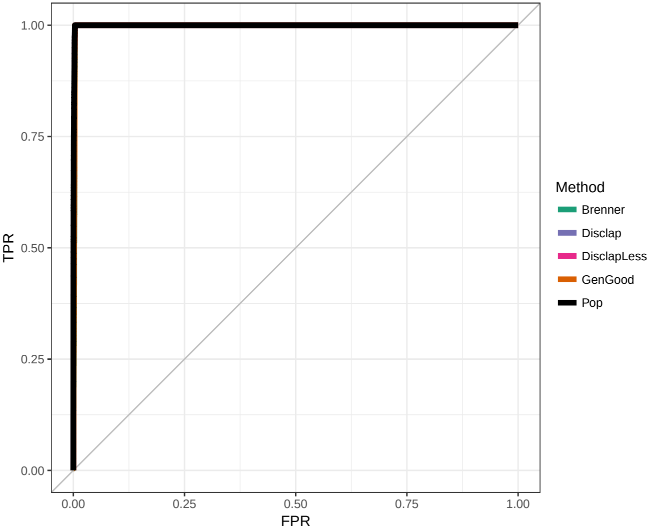


ROC

Rare/unobserved haplotypes

EU (N = 12,254; 5 loci; db n = 100)

All cases with k = 0 of sus.hap. in db. Grey line is the identity line, y = x.



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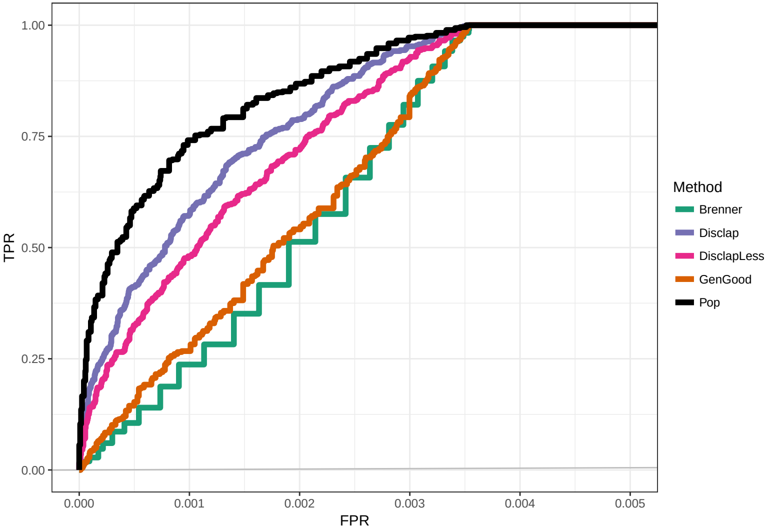

ROC

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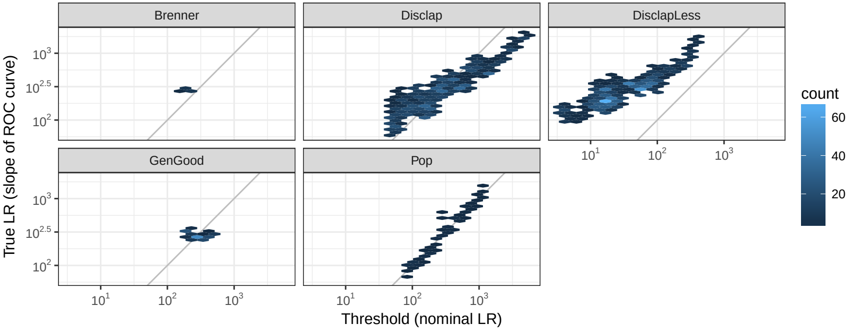
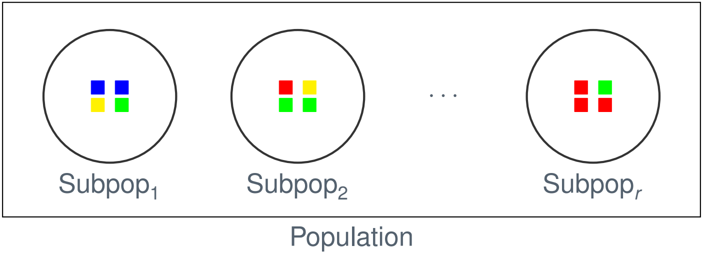


Slope of the tangent line at a point on the ROC curve gives the *LR* ('True *LR*') for that value/threshold of the test ('Threshold (nominal LR)').

Population substructure

Population substructure



Coloured squares represent haplotypes.

Random man (donor) and suspect belong to same subpopulation: Expected to share a haplotype more often than a random database sample from the whole population would represent.

θ (theta) correction: quantifies this; a remedy for not knowing the population substructure.

Estimating θ (theta)

Bruce Weir, pers. com. Assumptions apply.

- r: Number of subpopulations
- n_i: Size of reference database from i'th subpopulation ($i = 1, 2, \dots, r$)
- n_{ih}: Number of times haplotype h is observed in reference database from i'th subpopulation

$$m_i = \frac{1}{n_i(n_i - 1)} \sum_h n_{ih}(n_{ih} - 1) \quad \text{and} \quad m_{ij} = \frac{1}{n_i n_j} \sum_h n_{ih} n_{jh}$$

$$m_W = \frac{1}{r} \sum_{i=1}^{r} m_i \quad \text{and} \quad m_B = \frac{2}{r(r-1)} \sum_{i=1}^{r-1} \sum_{j=i+1}^{r} m_{ij}$$

$$\hat{\theta} = \frac{\frac{r-1}{r} \frac{m_W - m_B}{1 - m_B}}{1 - \frac{1}{r} \frac{m_W - m_B}{1 - m_B}} \overset{\text{large } r}{\approx} \frac{m_W - m_B}{1 - m_B}$$

Match probability

H_d: 'A random man **– that originate from the same subpopulation as the suspect –** left the Y-chromosome DNA in the crime stain.'

- Reference database from this subpopulation exists
  - Subpopulation is now the population
  - Use this reference database and no θ correction!
- Reference database from population with unknown population substructure:
  - One approach (based on the Balding-Nichols model): $P(E \mid H_d) \overset{BN}{=} \theta + (1 - \theta)p_h$
  - θ (theta) $(0 \leq \theta \leq 1)$
    - Population parameter (related to how much haplotype frequencies vary in different subpopulations)
    - Most simple model – many extensions possible

Match probability

$$P^{BN}(E \mid H_d) = \theta + (1-\theta)p_h$$

Note, that

$$P^{BN}(E \mid H_d) \geq \theta$$

and

$$P^{BN}(E \mid H_d) \geq p_h$$

- p_h really small compared to $\theta \Rightarrow P^{BN}(E \mid H_d) \approx \theta$
- p_h really large compared to $\theta \Rightarrow P^{BN}(E \mid H_d) \approx p_h$

	$p_h = 1/100{,}000$ = 0.00001	$p_h = 1/100 = 0.01$
$\theta = 0.001$	$P^{BN}(E \mid H_d)$ = 0.0010099	$P^{BN}(E \mid H_d)$ = 0.01099
$\theta = 0.003$	$P^{BN}(E \mid H_d)$ = 0.0030099	$P^{BN}(E \mid H_d)$ = 0.01297

Population substructure: Examples

Example 1: English reference database. We assume no population substructure (haplotype distribution same in the entire population).

- H_d: 'A random Englishman left the Y-chromosome DNA in the crime stain.'
- Use (estimate of) population frequency, p_h, based on English reference database (and no θ correction)

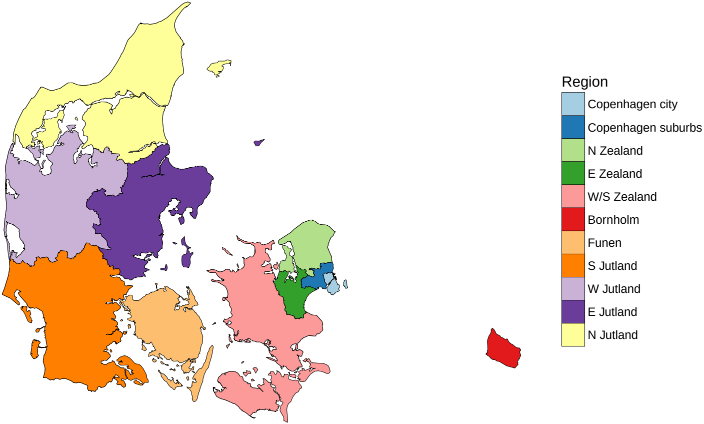
Example 2: English reference database. We assume population substructure (such that haplotype distribution may differ e.g. between regions).

- H_d: 'A random Englishman originating from the same region as the suspect left the Y-chromosome DNA in the crime stain.'
- Use θ correction: $\theta + (1 - \theta)p_h$ with θ estimated in advance using reference databases from comparable regions and (estimate of) population frequency, p_h, based on English reference database

Denmark

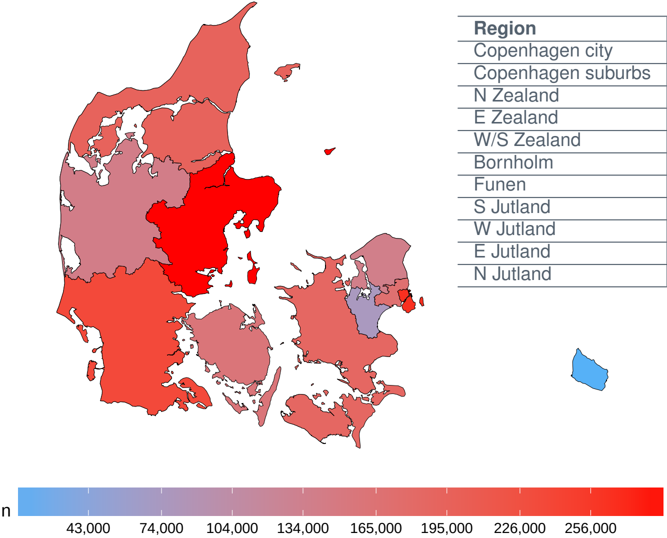
11 NUTS-3 (*nomenclature des unités territoriales statistiques*) regions

- The Danish Family Relations Database: ≈ 9,300,000
- Males: ≈ 4,700,000
- Men, alive, 15-65 years, known last residence: ≈ 1,900,000



Denmark

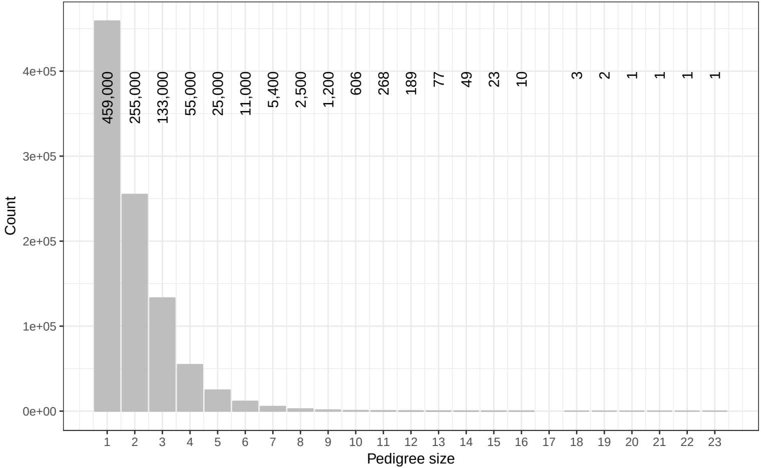
Region population sizes



Region	$n_{\text{males}} \approx$	**Area [km^2]**
Copenhagen city	250,000	150
Copenhagen suburbs	175,000	350
N Zealand	150,000	1,500
E Zealand	75,000	800
W/S Zealand	200,000	6,000
Bornholm	15,000	550
Funen	150,000	3,500
S Jutland	250,000	9,000
W Jutland	150,000	7,000
E Jutland	300,000	6,000
N Jutland	200,000	8,000

Denmark

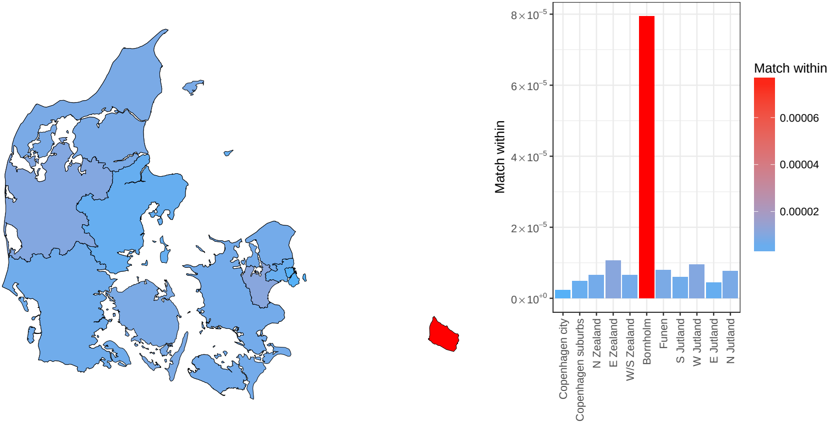
Pedigrees (males)



Denmark

Match within

$$\frac{1}{n_i(n_i-1)}\sum_h n_{ih}(n_{ih}-1)$$



θ (theta) Danish subdivisions

θ (theta) for 11 Danish NUTS-3 regions:

$$\theta = 1.2 \cdot 10^{-5}$$
$$\theta_{\text{weighted}} = 5.5 \cdot 10^{-6}$$

θ (theta) for 99 Danish local authorities/municipalities:

$$\theta = 4.1 \cdot 10^{-4}$$
$$\theta_{\text{weighted}} = 4.2 \cdot 10^{-5}$$

θ_{weighted}: means weighted by subpopulation sizes.

(Based on – possibly incomplete – pedigree information, no genetic information.)

Thank you for your attention

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[AEM13] Mikkel Meyer Andersen, Poul Svante Eriksen, and Niels Morling. The discrete Laplace exponential family and estimation of Y-STR haplotype frequencies. *Journal of Theoretical Biology*, 329:39–51, 2013.

[AEM14] Mikkel Meyer Andersen, Poul Svante Eriksen, and Niels Morling. Cluster analysis of European Y-chromosomal STR haplotypes using the discrete Laplace method. *Forensic Science International: Genetics*, 11:182–194, 2014.

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[Bre10] Charles H. Brenner. Fundamental problem of forensic mathematics – The evidential value of a rare haplotype. *Forensic Science International: Genetics*, 4(5):281–291, 2010.

[Cer15] Giulia Cereda. Non parametric Bayesian approach to LR assessment in case of rare haplotype match. *arXiv:1506.08444*, (in preparation), 2015.

[Cer17] Giulia Cereda. Impact of model choice on LR assessment in case of rare haplotype match (frequentist approach). *Scandinavian Journal of Statistics*, (to appear), 2017.