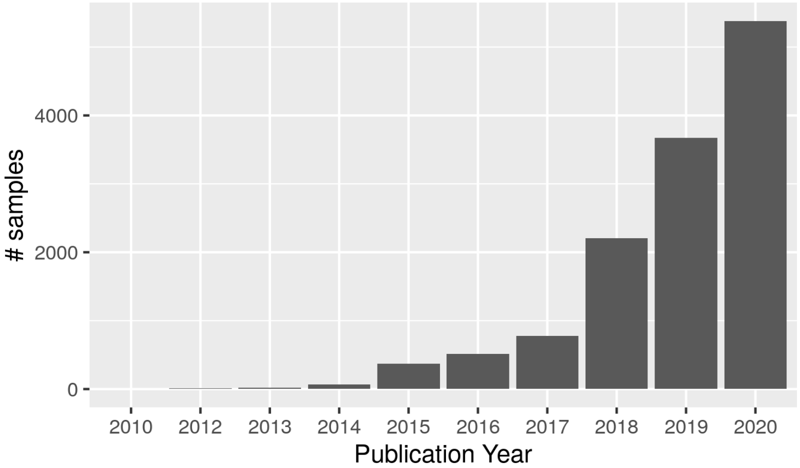
F-statistics and PCA

Benjamin Peter

April 21, 2021

Population structure and ancient DNA



https://reich.hms.harvard.edu/

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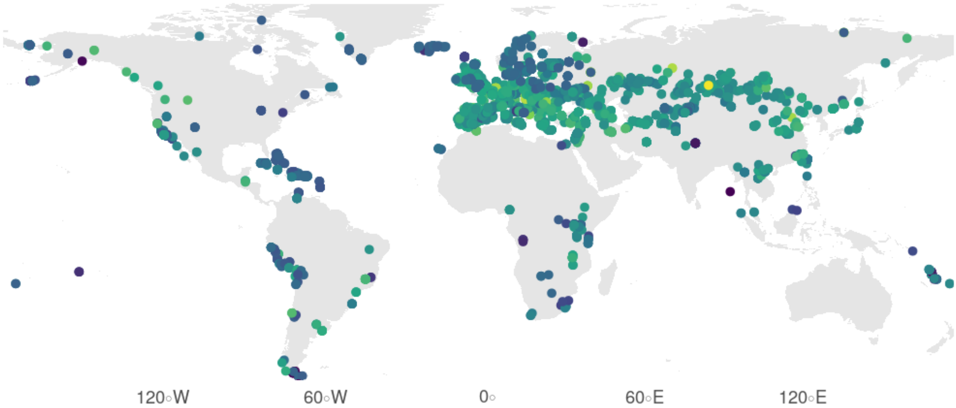

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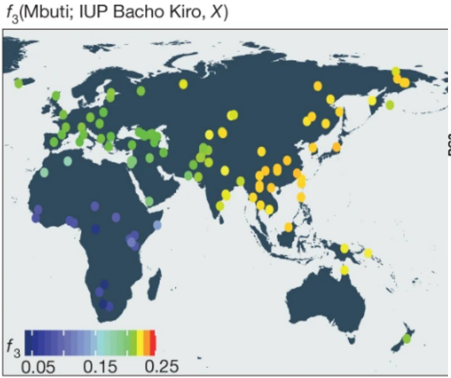
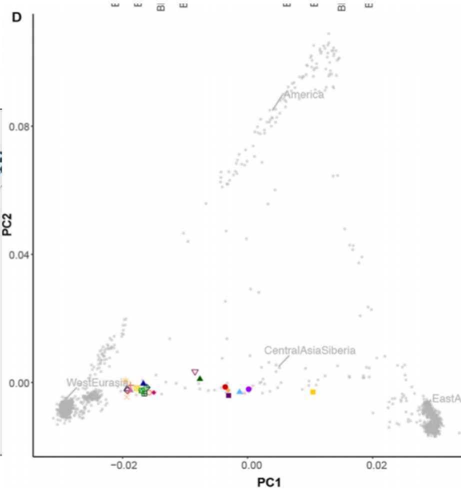
PCA and F-statistics





Hajdinjak et al. 2021

Goals of this talk

- Technical & Conceptual Background
- Establish conceptual links between frameworks
  1. How can we interpret PCA in context of F-stats?
  2. How can we interpret F-stats in the context of PCA?
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Focus on intuition

Some details in terms of estimation, normalization, missing data will be glossed over

F-statistics

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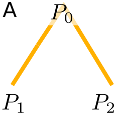
$F_2(X_1, X_2) = \sum_l (X_{il} - X_{jl})^2 - H_1 - H_2$	A 

Patterson et al. 2012; Peter 2016

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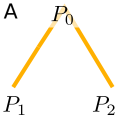
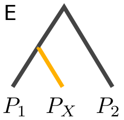
$$F_2(X_1, X_2) = \sum_l (X_{il} - X_{jl})^2 - H_1 - H_2$$	A 
$$F_3(X_x; X_1, X_2) = \sum_l (X_{xl} - X_{1l})(X_{xl} - X_{2l}) - H_X$$ $$F_3(X_x; X_1, X_2) = F_2(X_x, X_1) + F_2(X_x, X_2) - F_2(X_1, X_2)$$	E 

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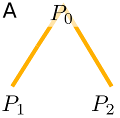
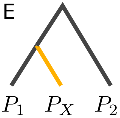
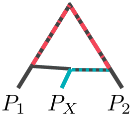
$$F_2(X_1, X_2) = \sum_l (X_{il} - X_{jl})^2 - H_1 - H_2$$	
$$F_3(X_x; X_1, X_2) = \sum_l (X_{xl} - X_{1l})(X_{xl} - X_{2l}) - H_X$$ $$F_3(X_x; X_1, X_2) = F_2(X_x, X_1) + F_2(X_x, X_2) - F_2(X_1, X_2)$$	
"Admixture"-F_3-statistic: If data is generated by a tree-like relationship, $F_3(P_X; P_1, P_2) \geq 0$	

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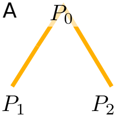
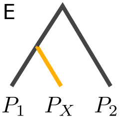
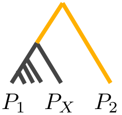
$$F_2(X_1, X_2) = \sum_l (X_{il} - X_{jl})^2 - H_1 - H_2$$	
$$F_3(X_x; X_1, X_2) = \sum_l (X_{xl} - X_{1l})(X_{xl} - X_{2l}) - H_X$$ $$F_3(X_x; X_1, X_2) = F_2(X_x, X_1) + F_2(X_x, X_2) - F_2(X_1, X_2)$$	
"Outgroup"-F_3-statistic: Most similar pops have highest $F_3(P_2; P_X, P_1)$	

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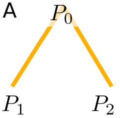
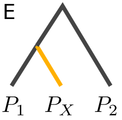
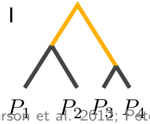
$$F_2(X_1, X_2) = \sum_l (X_{il} - X_{jl})^2 - H_1 - H_2$$	
$$F_3(X_x; X_1, X_2) = \sum_l (X_{xl} - X_{1l})(X_{xl} - X_{2l}) - H_X$$ $$F_3(X_x; X_1, X_2) = F_2(X_x, X_1) + F_2(X_x, X_2) - F_2(X_1, X_2)$$	
$$F_4^{(B)}(X_1; X_2; X_3, X_4) = \sum_l (X_{1l} - X_{3l})(X_{2l} - X_{4l})$$	

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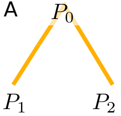

$$F_3(X_x; X_1, X_2) = \sum_l (X_{xl} - X_{1l})(X_{xl} - X_{2l}) - H_X$$

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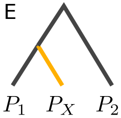
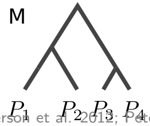


$$F_4^{(T)}(X_1; X_2; X_3, X_4) == \sum_l (X_{1l} - X_{2l})(X_{3l} - X_{4l})$$

M



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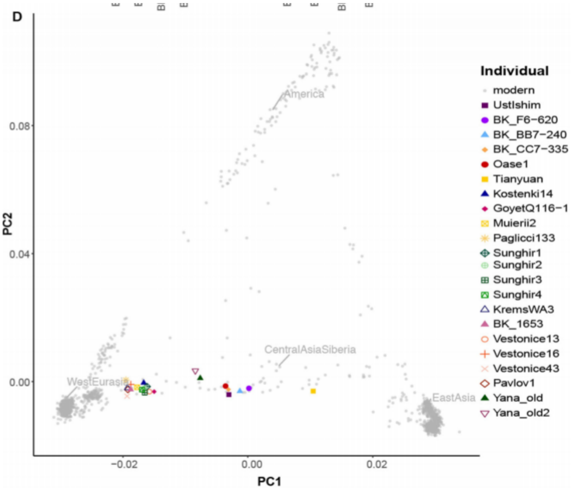
Principal Component Analysis



McVean, 2009

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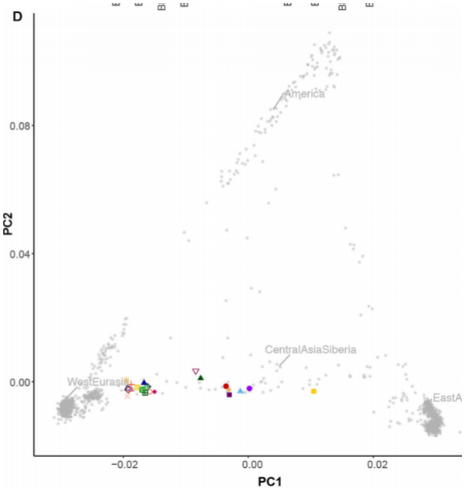

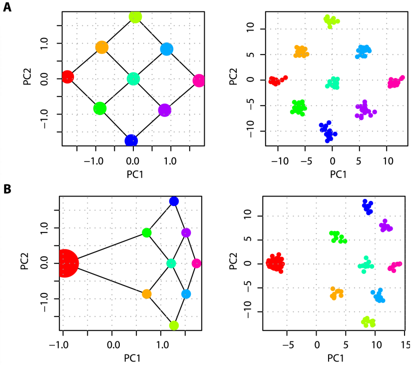

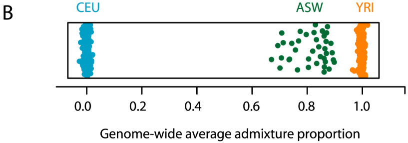

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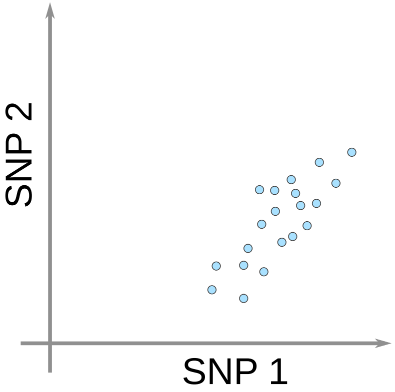

- Raw SNP data $\mathbf{X}$; x_{ij}

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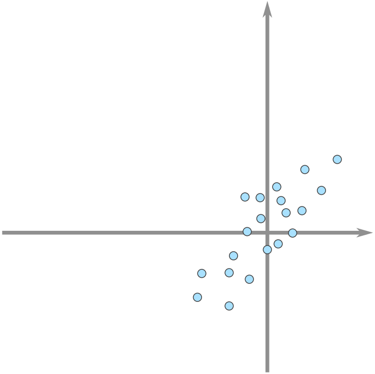

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  $\mathbf{Y} = \mathbf{CX}$; $y_{ij} = x_{ij} - \mu_j$

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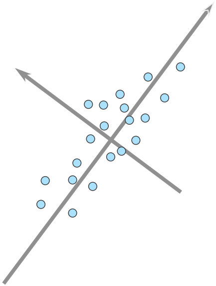

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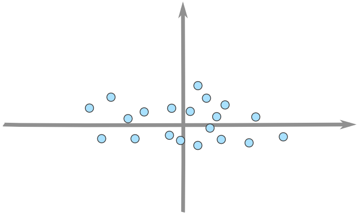

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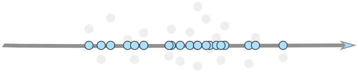

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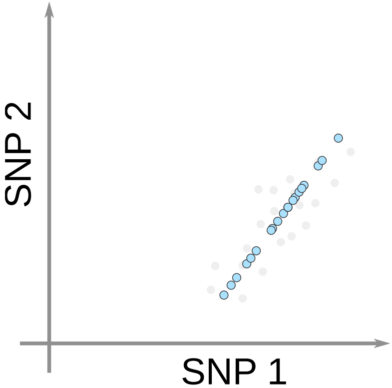

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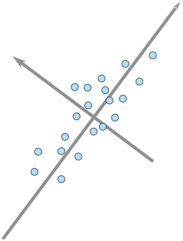
How to find PCs



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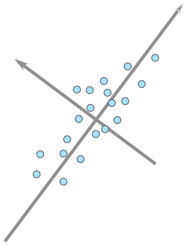

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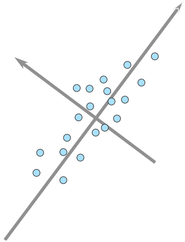

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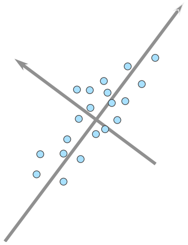

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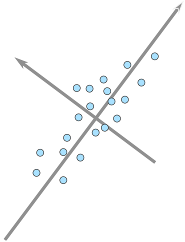

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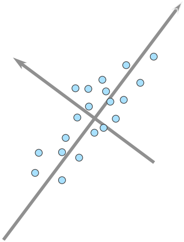

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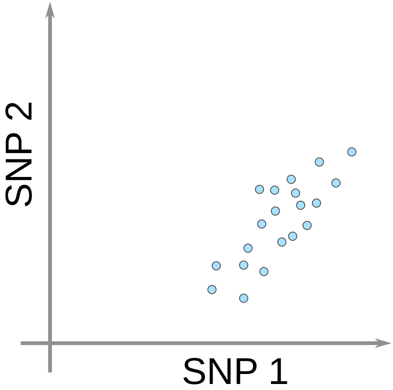
Observation

PCA is equivalent to outgroup-F_3-analysis with sample mean as outgroup

(metric) Multi-Dimensional Scaling (MDS)



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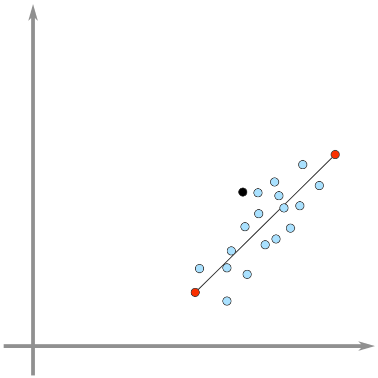

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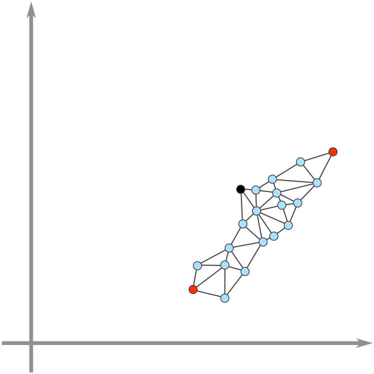

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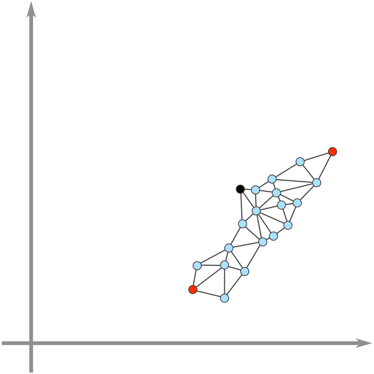

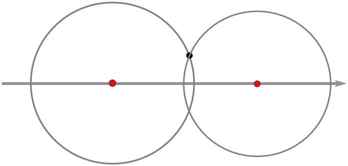

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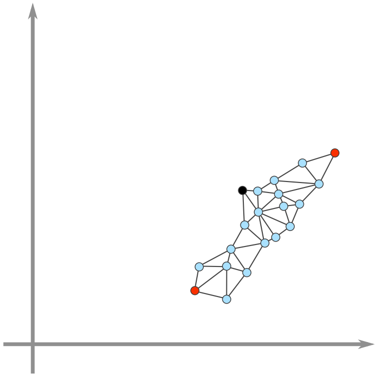

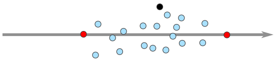

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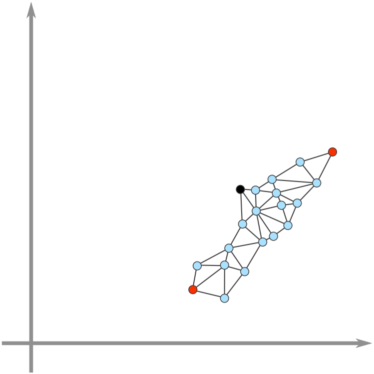

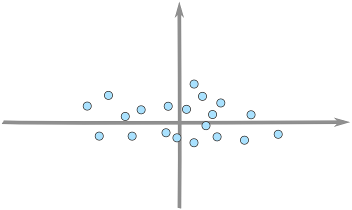

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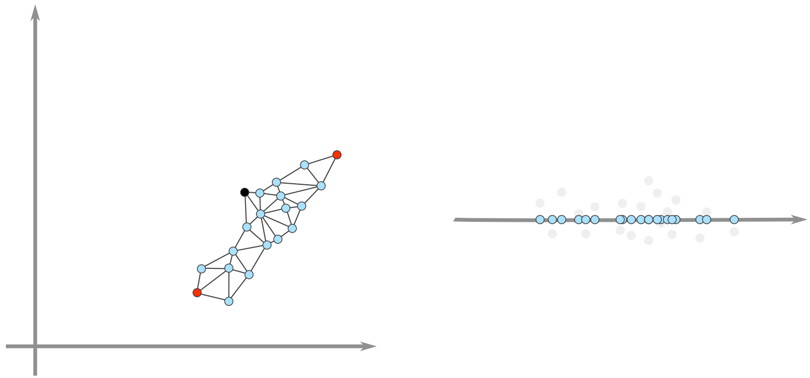

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Observation

PCA is equivalent to MDS on $\mathbf{F}_2$

PCA is MDS on Outgroup$\mathbf{F}_3$

- PCA is decomposition of Covariance matrix: $\mathbf{Y}\mathbf{Y}^T$

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- Consider $\mathbf{F}_3(O)$; $f_{ij} = F_3(O; X_i, X_j) = O^2 - OX_i - OX_j + X_iX_j$

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- PCA is decomposition of Covariance matrix: $\mathbf{YY}^T$
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Observation

Decomposition of *any* centered F_3-matrix is equivalent to PCA.

0-diagonal MDS

F-statistics on PCA-plot

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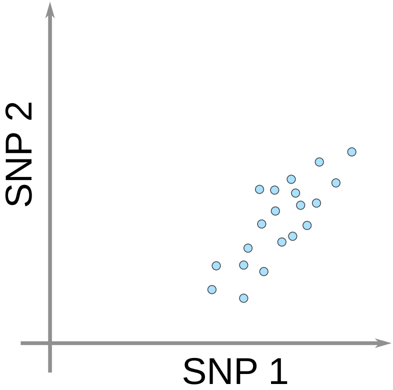
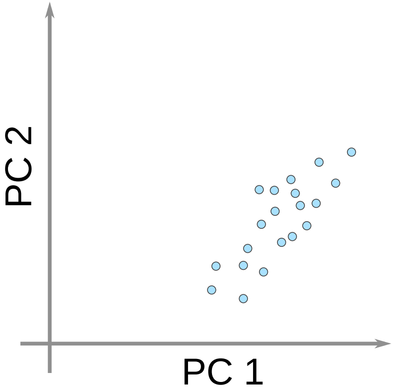
Observation

F_2 can be decomposed in contributions of different principal components

F-statistics on PCA-plot



F-statistics on PCA-plot



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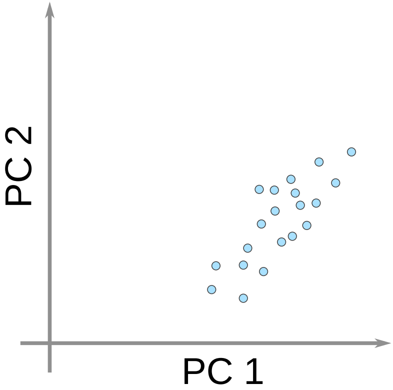

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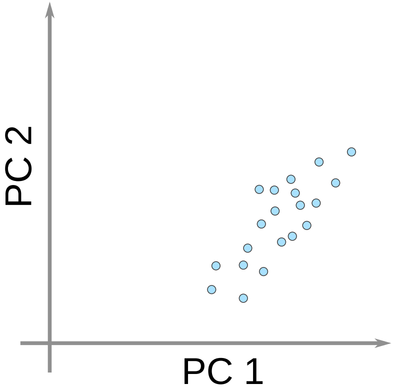
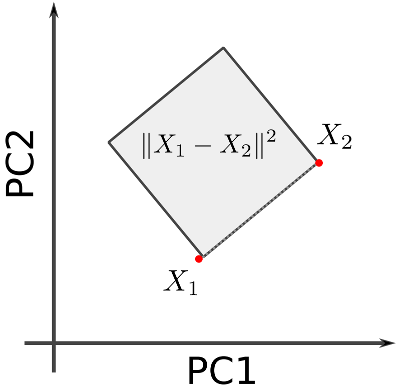


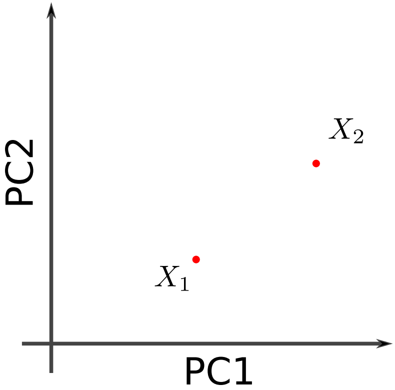
- F-statistics have a geometrical representation on PCA-plot
- Exact only if we use *all* PCs
- Good approximation for 2D-plot if first 2 PCs capture relevant population structure

F_2-statistic on PCA-plot



- $F_2(X_1, X_2) = \sum_l (X_{1l} - X_{2l})^2$
- $F_2(X_1, X_2) = \|X_1, X_2\|^2$

Admixed populations (F_3) on PCA-plot



- Given X_1, X_2, which pops have $F_3 < 0$?

McVean 2009

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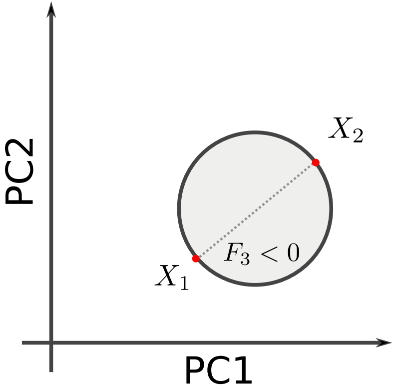

- Given X_1, X_2, which pops have $F_3 < 0$?
- $F_3(Y; X_1, X_2) = 0$ is a circle!

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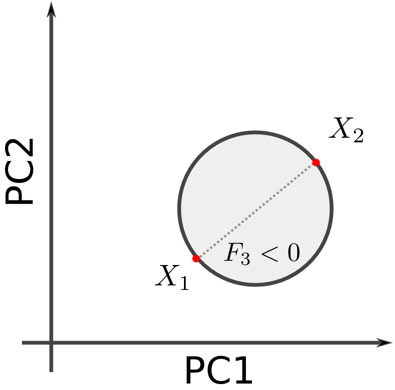

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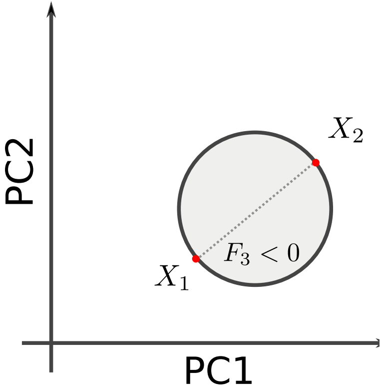

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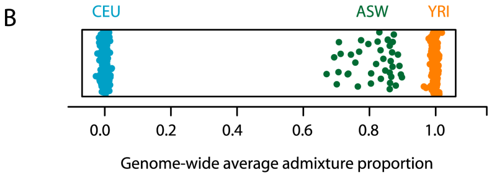

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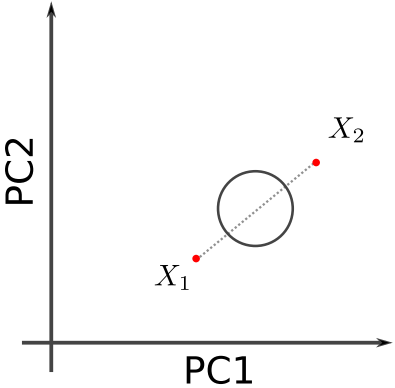
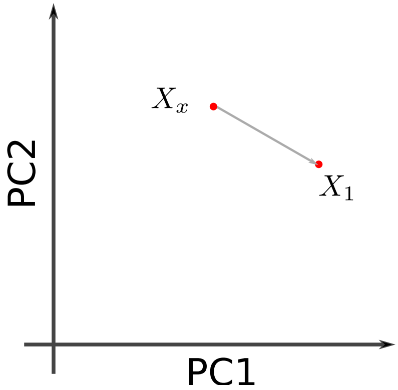


- Given X_1, X_2, which pops have $F_3 < 0$?
- $F_3(Y; X_1, X_2) = 0$ is a circle!
- Samples outside circle will always have positive F_3
- $F_3(Y; X_1, X_2) = k < 0$ is smaller circle

McVean 2009

Admixture F_3-stats on PCA-plot



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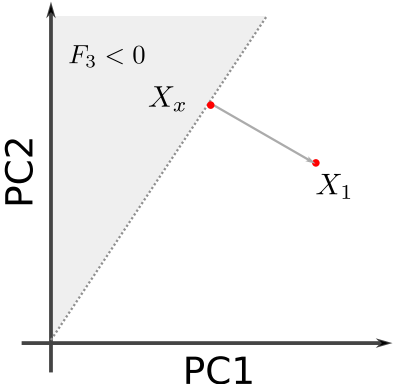

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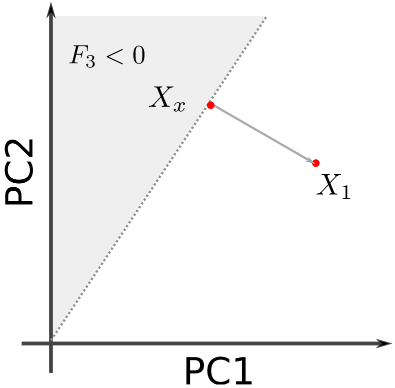

- Given X_1, X_x, which pops X_2 have $F_3 < 0$?
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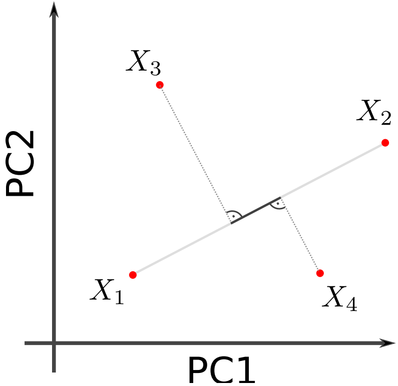
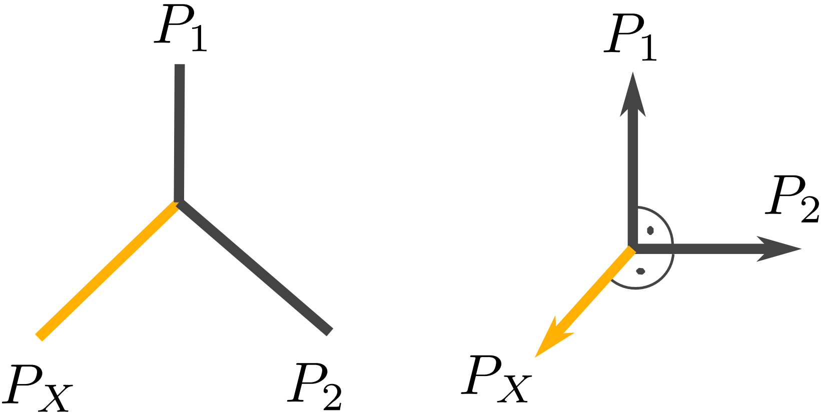
- Inner (dot) product: $F_3(X_x; X_1, X_2) = \langle X_x - X_1, X_x - X_2 \rangle$

F_4-stats on PCA-plot



- F_4 is projection of $\overline{X_3X_4}$ on $\overline{X_1X_2}$

Where does Orthogonality come from?



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   - use Dimensions / Orthogonality for useful data representations

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5. Better out-of-sample predictions
   - `qpGraph` and other tools fail with large samples