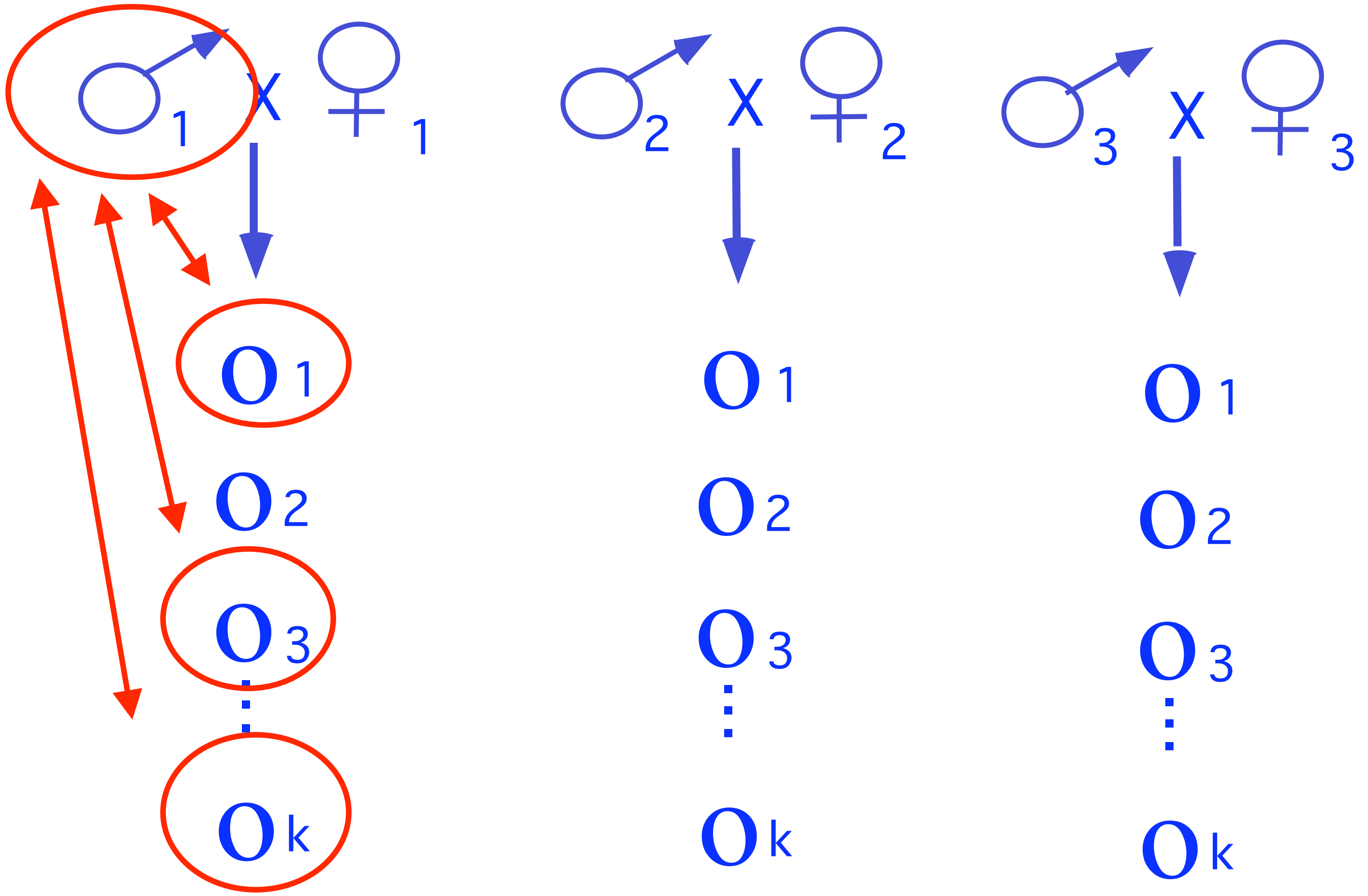
Lecture 7: Resemblance Between Relatives

Bruce Walsh lecture notes
Uppsala EQG 2012 course
version 28 Jan 2012

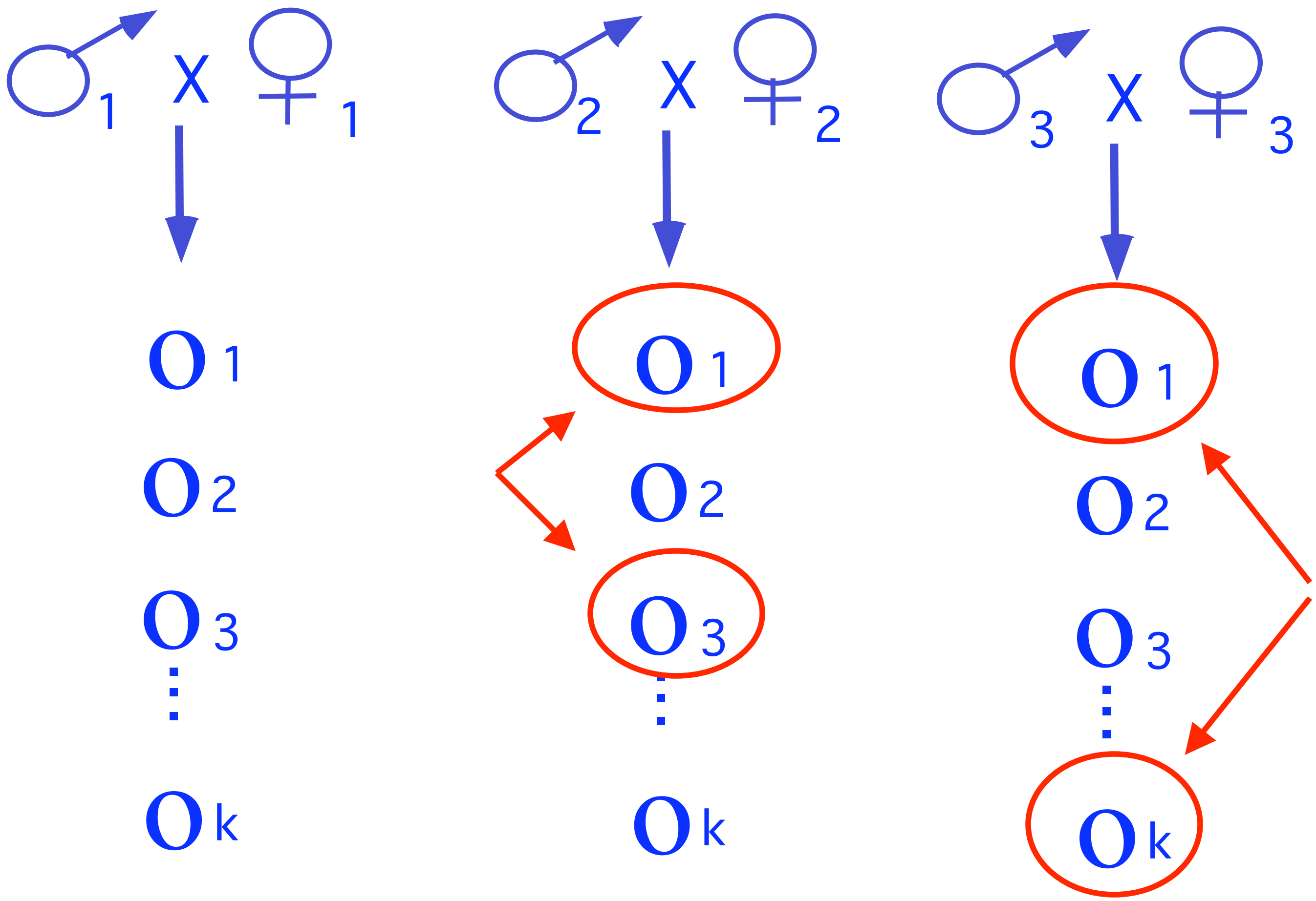
Heritability

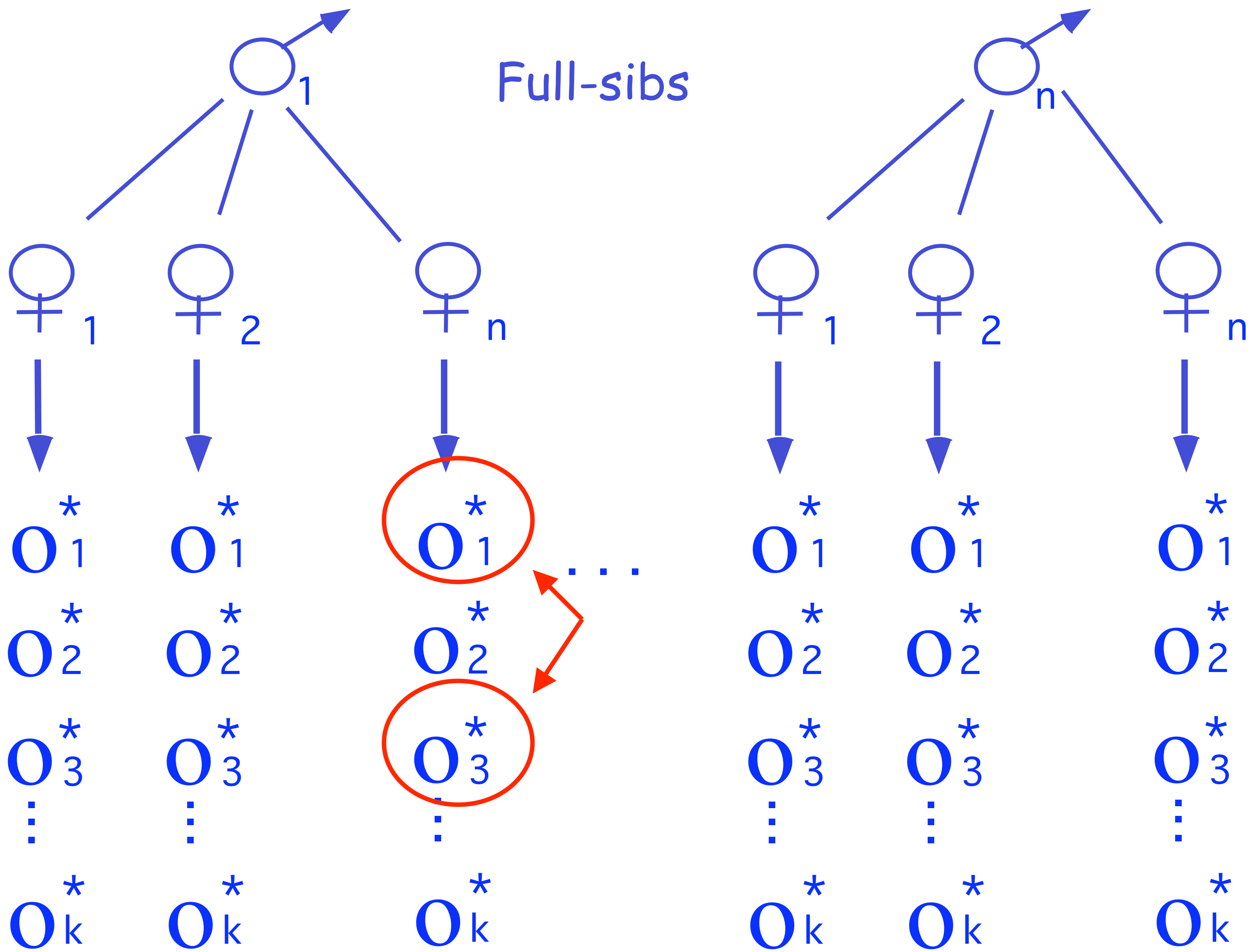
- Central concept in quantitative genetics
- Proportion of variation due to additive genetic values (Breeding values)
  - $h^2 = V_A/V_P$
  - Phenotypes (and hence V_P) can be directly measured
  - Breeding values (and hence V_A) must be estimated
- Estimates of V_A require known collections of relatives

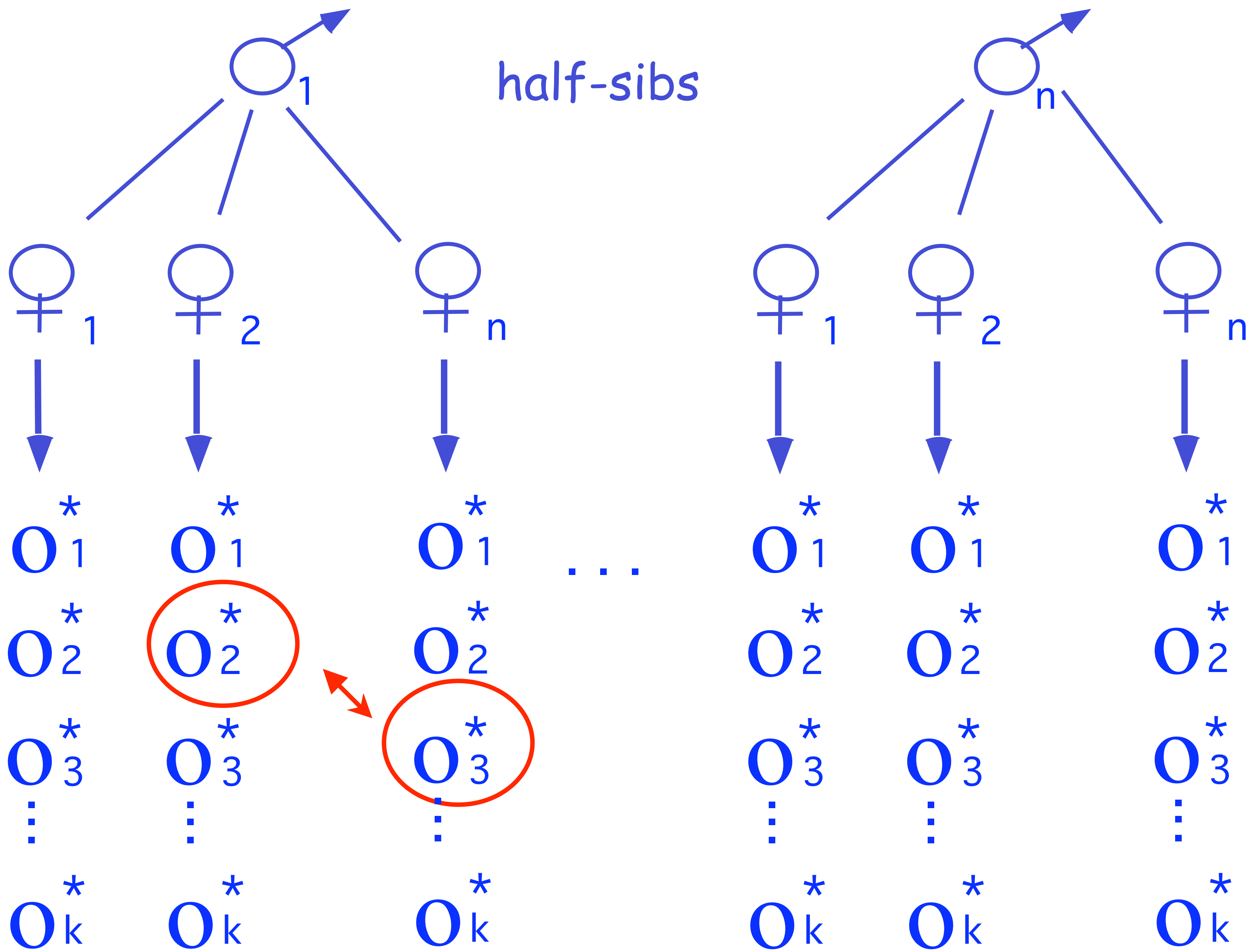
Ancestral relatives e.g., parent and offspring



Collateral relatives e.g. sibs




Full-sibs
1
n
1
2
n
1
2
n
O*1
O*2
O*3
O*k
. . .



half-sibs
1
n
1
2
n
1
2
n
O^*_1
O^*_2
O^*_3
O^*_k
. . .

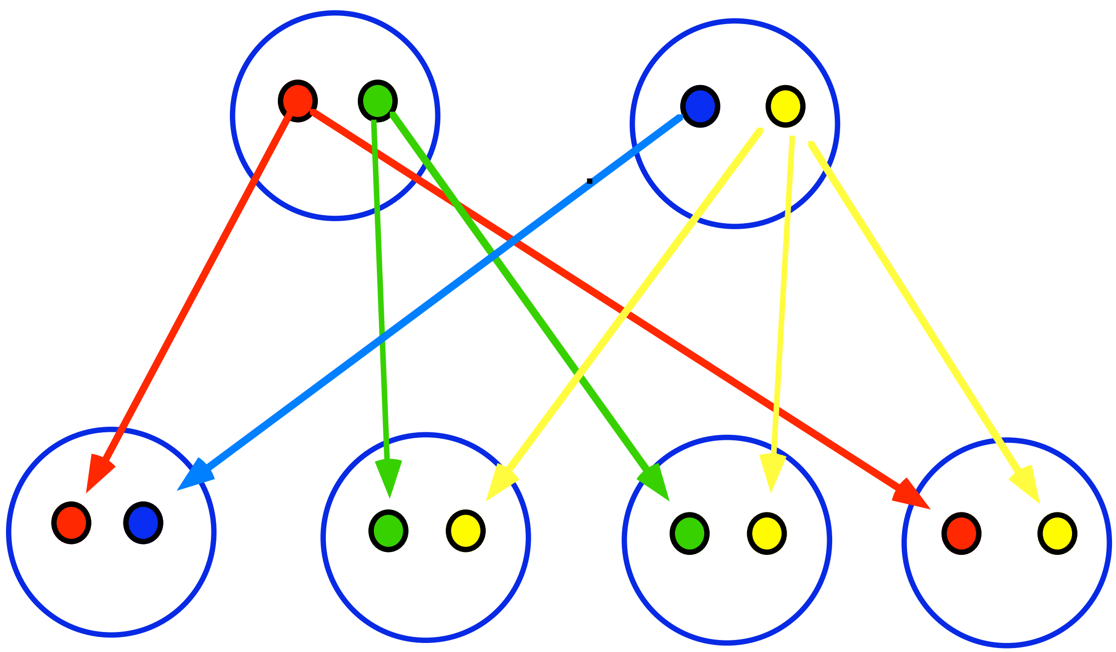
Key observations

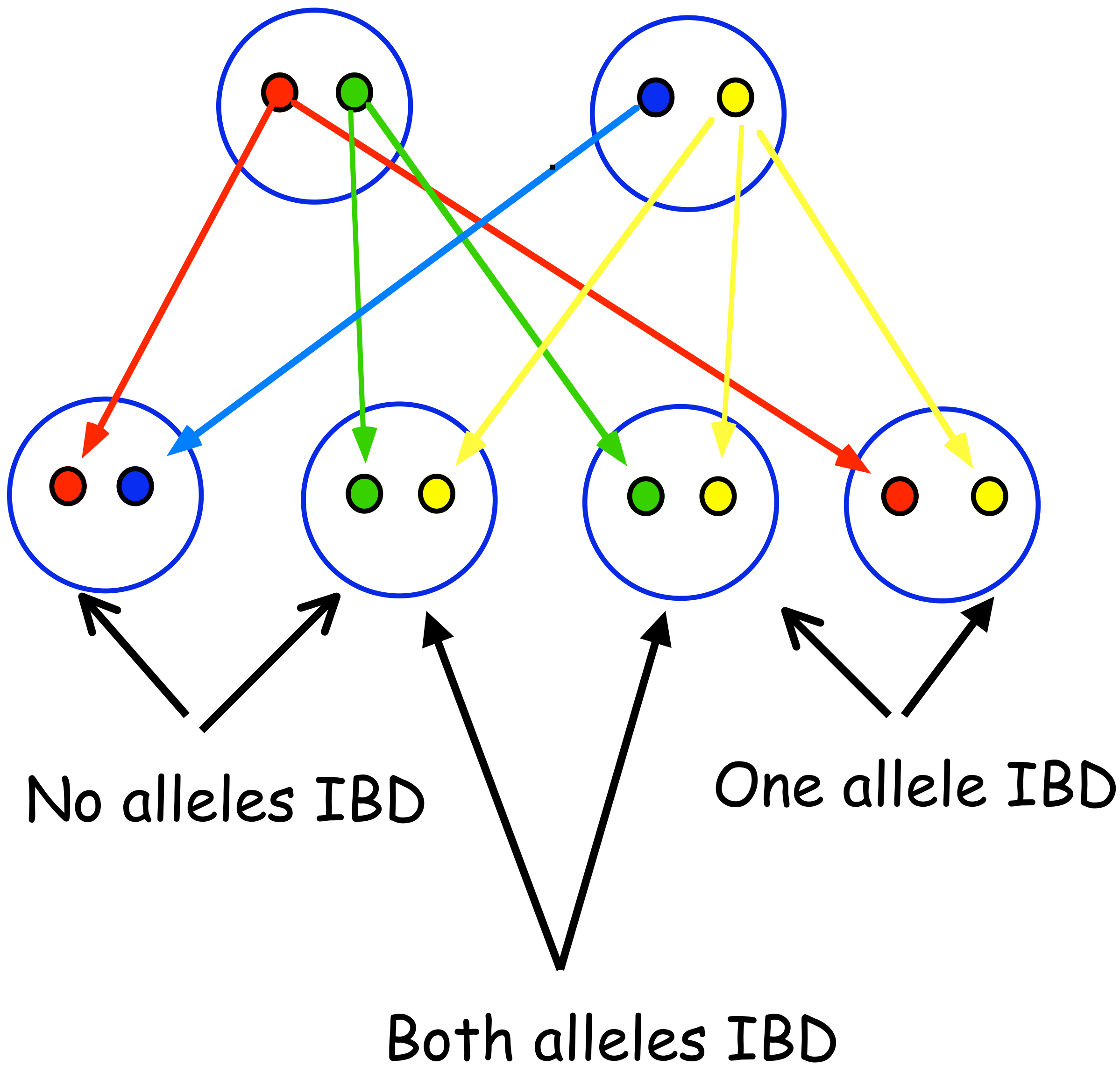
- The amount of phenotypic resemblance among relatives for the trait provides an indication of the amount of genetic variation for the trait.
- If trait variation has a significant genetic basis, the closer the relatives, the more similar their appearance

Genetic Covariance between relatives

Sharing alleles means having alleles that are identical by descent (IBD): both copies of can be traced back to a single copy in a recent common ancestor.

Genetic covariances arise because two related individuals are more likely to share alleles than are two unrelated individuals.




No alleles IBD
One allele IBD
Both alleles IBD

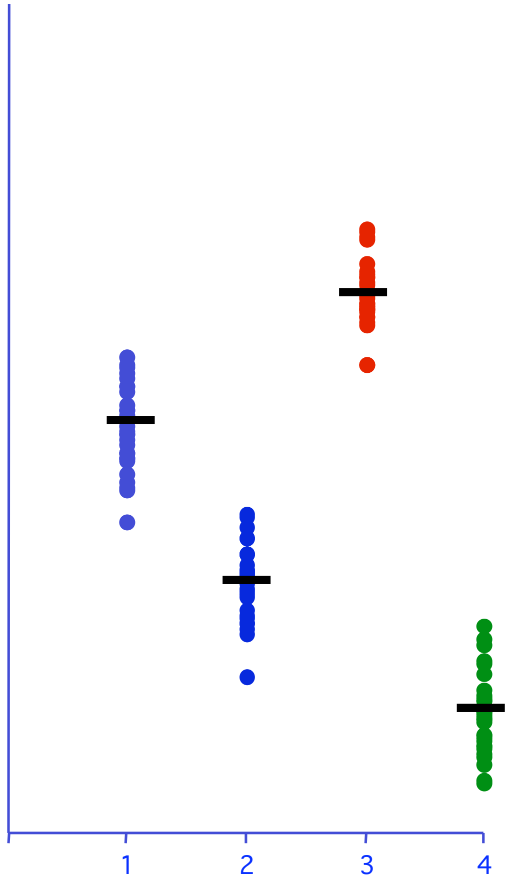
Regressions and ANOVA

- Parent-offspring regression
  - Single parent vs. midparent
  - Parent-offspring covariance is a interclass (between class) variance
- Sibs
  - Covariances between sibs is an intraclass (within class) variance

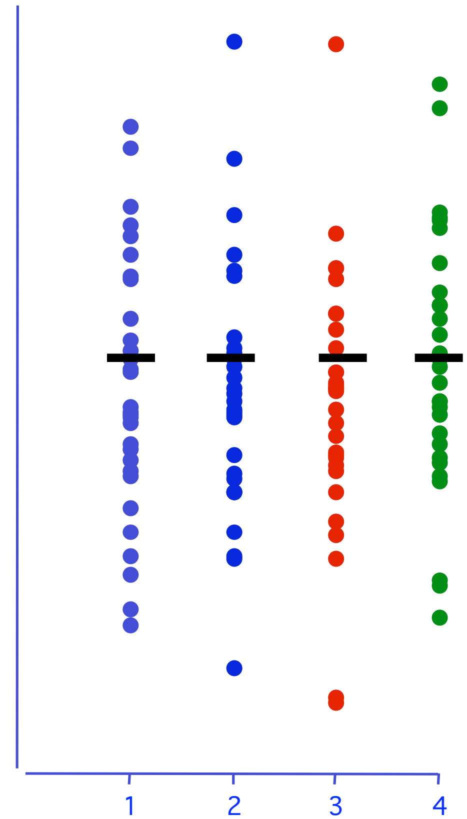
ANOVA

- Two key ANOVA identities
  - Total variance = between-group variance + within-group variance
    - Var(T) = Var(B) + Var(W)
  - Variance(between groups) = covariance (within groups)
  - Intraclass correlation, t = Var(B)/Var(T)

Situation 1



Situation 2



Var(B) = 2.5

Var(W) = 0.2 t = 2.5/2.7 = 0.93

Var(T) = 2.7

Var(B) = 0

Var(W) = 2.7 t = 0

Var(T) = 2.7

Parent-offspring genetic covariance

$Cov(G_p, G_o)$ --- Parents and offspring share EXACTLY one allele IBD

Denote this common allele by A_1

$$G_p = A_p + D_p = \alpha_1 + \alpha_x + D_{1x}$$

$$G_o = A_o + D_o = \alpha_1 + \alpha_y + D_{1y}$$

IBD allele

Non-IBD alleles

$$
\begin{aligned}
Cov(G_o, G_p) &= Cov(\alpha_1 + \alpha_x + D_{1x}, \alpha_1 + \alpha_y + D_{1y}) \\
&= Cov(\alpha_1, \alpha_1) + Cov(\alpha_1, \alpha_y) + Cov(\alpha_1, D_{1y}) \\
&+ Cov(\alpha_x, \alpha_1) + Cov(\alpha_x, \alpha_y) + Cov(\alpha_x, D_{1y}) \\
&+ Cov(D_{1x}, \alpha_1) + Cov(D_{1x}, \alpha_y) + Cov(D_{1x}, D_{1y})
\end{aligned}
$$

All blue covariance terms are zero.

- By construction, α and D are uncorrelated
- By construction, α from non-IBD alleles are uncorrelated
- By construction, D values are uncorrelated unless both alleles are IBD

$$Cov(\alpha_x, \alpha_y) = \begin{cases} 0 & \text{if } x \neq y, \quad \text{i.e., not IBD} \\ Var(A)/2 & \text{if } x = y, \quad \text{i.e., IBD} \end{cases}$$

$$Var(A) = Var(\alpha_1 + \alpha_2) = 2Var(\alpha_1)$$

so that

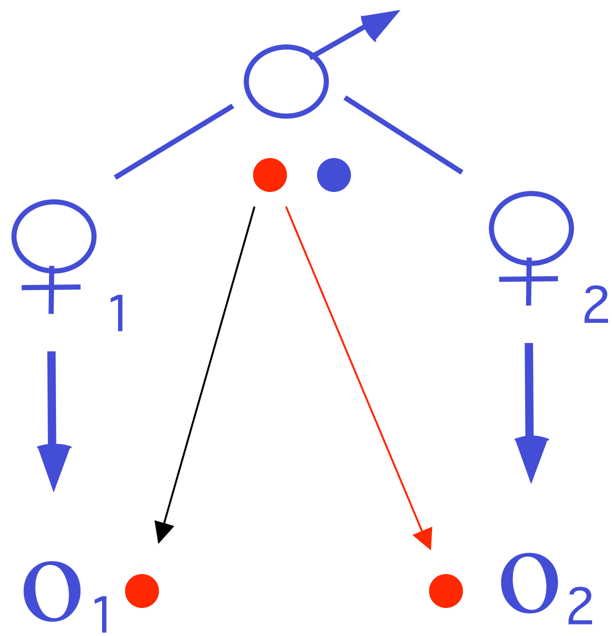
$$Var(\alpha_1) = Cov(\alpha_1, \alpha_1) = Var(A)/2$$

Hence, relatives sharing one allele IBD have a genetic covariance of Var(A)/2

The resulting parent-offspring genetic covariance becomes $Cov(G_p, G_o) = Var(A)/2$

Half-sibs

Each sib gets exactly one allele from common father, different alleles from the different mothers

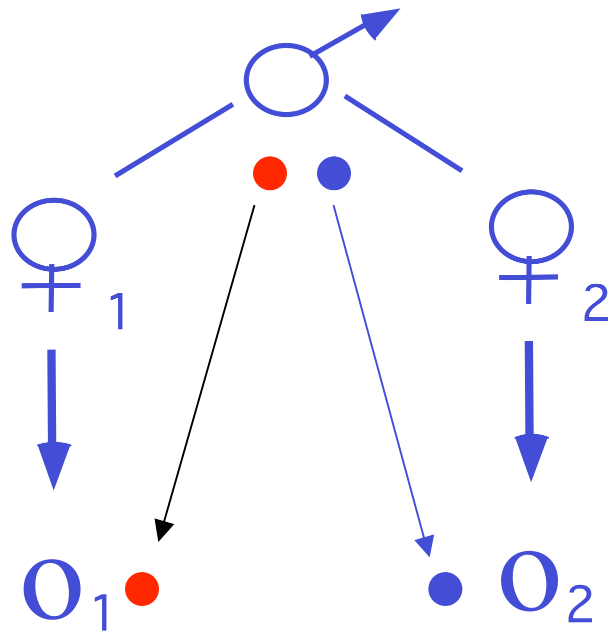


The half-sibs share one allele IBD

- occurs with probability 1/2

Half-sibs

Each sib gets exactly one allele from common father, different alleles from the different mothers

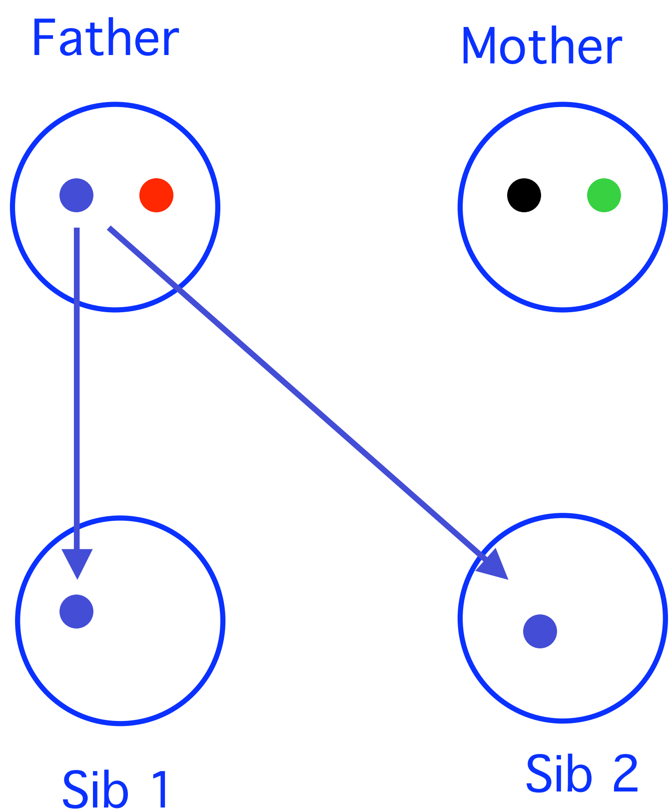


The half-sibs share no alleles IBD

- occurs with probability 1/2

Hence, the genetic covariance of half-sibs is just (1/2)Var(A)/2 = Var(A)/4

Full-sibs



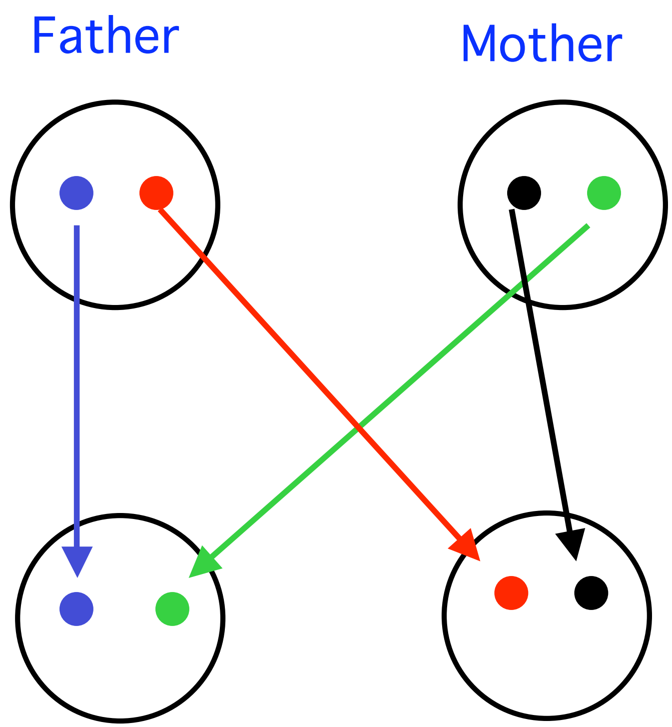
Each sib gets exact one allele from each parent

Prob(Allele from father IBD) = 1/2. Given the allele in parent one, prob = 1/2 that sib 2 gets same allele

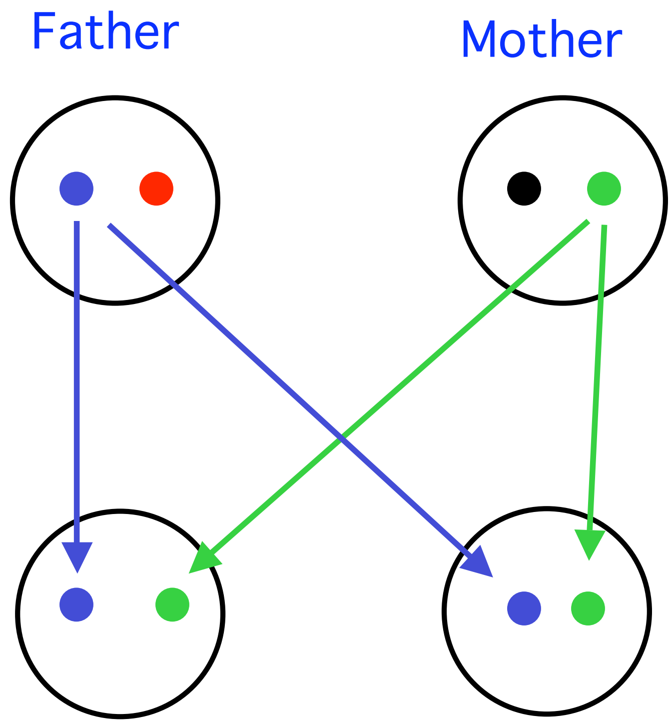
Prob(Allele from father not IBD) = 1/2. Given the allele in parent one, prob = 1/2 that sib 2 gets different allele

Full-sibs

Each sib gets exact one allele from each parent



Paternal allele not IBD [Prob = 1/2]
Maternal allele not IBD [Prob = 1/2]
Prob(sibs share 0 alleles IBD) = 1/2*1/2 = 1/4



Each sib gets
exact one allele
from each parent

Paternal allele IBD [Prob = 1/2]

Maternal allele IBD [Prob = 1/2]

Prob(sibs share 2 alleles IBD) = 1/2*1/2 = 1/4

Prob(share 1 allele IBD) = 1-Pr(0) - Pr(2) = 1/2

Resulting Genetic Covariance between full-sibs

IBD alleles	Probability	Contribution
0	1/4	0
1	1/2	Var(A)/2
2	1/4	Var(A) + Var(D)

Cov(Full-sibs) = Var(A)/2 + Var(D)/4

Genetic Covariances for General Relatives

Let r = (1/2)Prob(1 allele IBD) + Prob(2 alleles IBD)

Let u = Prob(both alleles IBD)

General genetic covariance between relatives

$$Cov(G) = rVar(A) + uVar(D)$$

When epistasis is present, additional terms appear

$$r^2Var(AA) + ruVar(AD) + u^2Var(DD) + r^3Var(AAA) +$$

Components of the Environmental Variance

Total environmental value

Specific environmental value, any unique environmental effects experienced by the individual

$$E = E_c + E_s$$

Common environmental value experienced by all members of a family, e.g., shared maternal effects

The Environmental variance can thus be written in terms of variance components as

$$V_E = V_{Ec} + V_{Es}$$

One can decompose the environmental further, if desired. For example, plant breeders have terms for the location variance, the year variance, and the location x year variance.

Shared Environmental Effects contribute to the phenotypic covariances of relatives

$$Cov(P_1,P_2) = Cov(G_1+E_1,G_2+E_2)$$
$$= Cov(G_1,G_2) + Cov(E_1,E_2)$$

Shared environmental values are expected when sibs share the same mom so that Cov(Full sibs) and Cov(Maternal half-sibs) not only contain a genetic covariance, but an environmental covariance as well, V_{Ec}

$$Cov(\text{Full-sibs}) = Var(A)/2 + Var(D)/4 + V_{Ec}$$

Coefficients of Coancestry

Suppose we pick a single allele each at random from two relatives. The probability that these are IBD is called Θ, the coefficient of coancestry

Θ_{xy} denotes the coefficient for relatives x and y

Consider an offspring z from a (hypothetical) cross of x and y. $\Theta_{xy} = f_z$, the inbreeding coefficient of z

Θ_{xx}: The Coancestry of an individual with itself

Self x, what is the inbreeding coefficient of its offspring?

To compute Θ_{xx}, denote the two alleles in x by A_1 and A_2

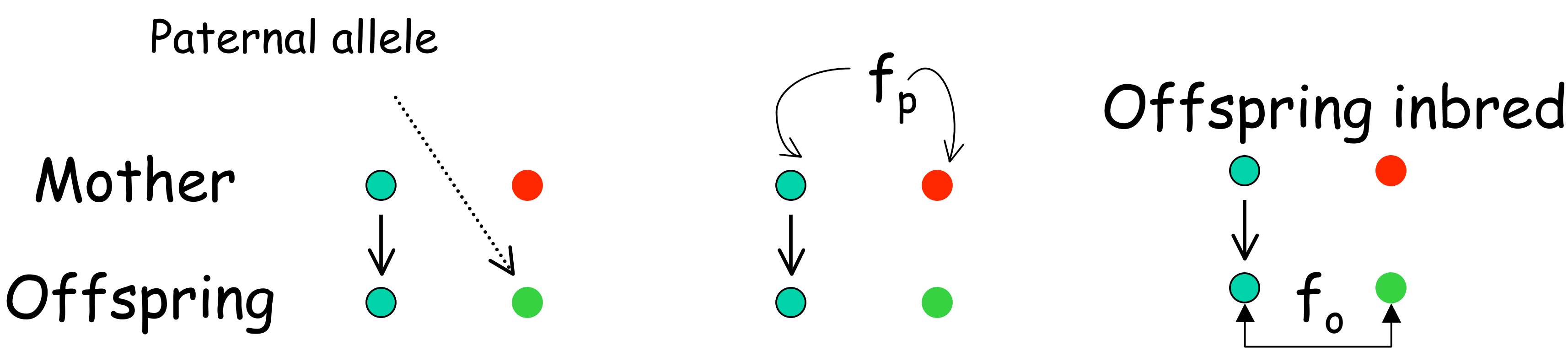
	Draw A_1	Draw A_2
Draw A_1	IBD	f_x
Draw A_2	f_x	IBD

Hence, for a non-inbred individual, $\Theta_{xx} = 2/4 = 1/2$

If x is inbred, f_x = prob A_1 and A_2 IBD, $\Theta_{xx} = (1+ f_x)/2$

Θ_{op} = Parent & Offspring

Parent inbred



$$\theta_{po} = \frac{1}{4}$$

$$\theta_{po} = \frac{1+f_p}{4}$$

$$\theta_{po} = \frac{1+2f_o}{4}$$

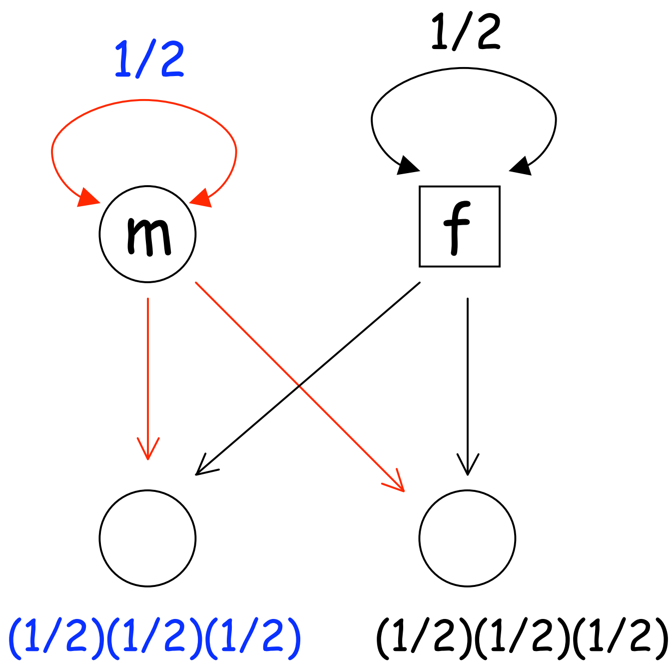
1/2 = Prob random offspring allele from father. Prob = θ_{mf} = f_o that this allele is IBD to mother giving a contribution of $f_o/2$

$$\theta_{po} = \frac{1}{4}(1 + f_p + 2f_o)$$

← θ_{mf}

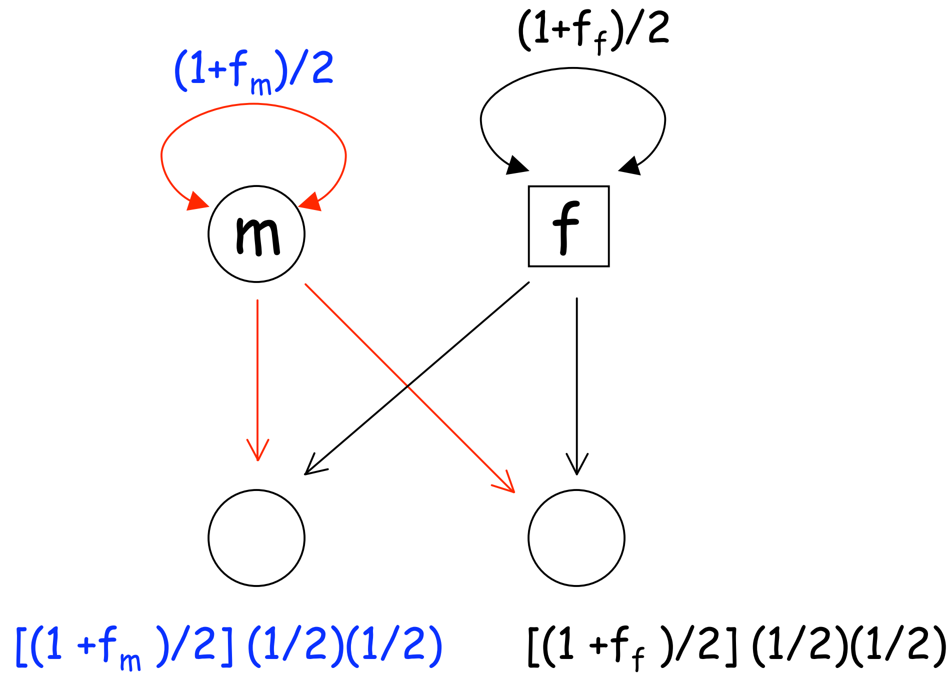
Full sibs (x and y) from parents m and f

$\Theta = 1/8 + 1/8 = 1/4$



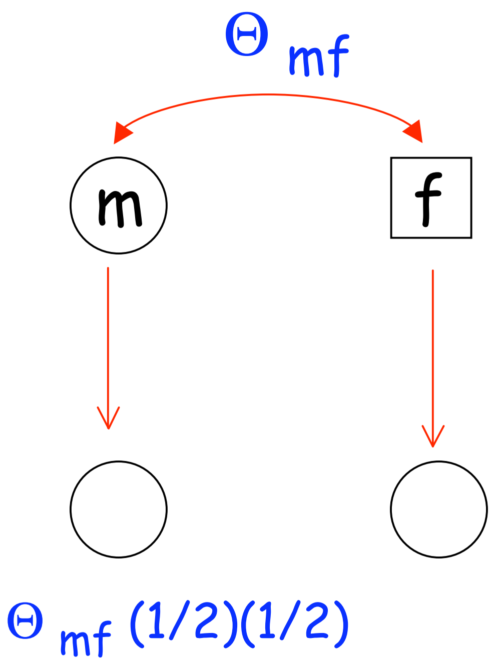
Unrelated, non-inbred parents

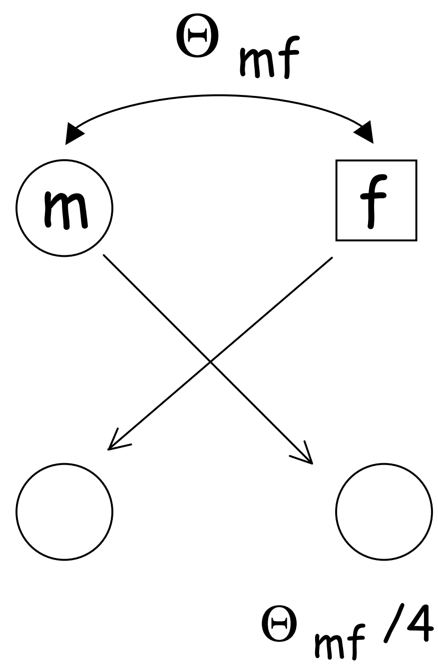
$\Theta = (2+f_m+f_f)/8$



Unrelated, inbred parents

Full sibs (x and y) from parents m and f





Parents inbred & related.

Two additional paths to add

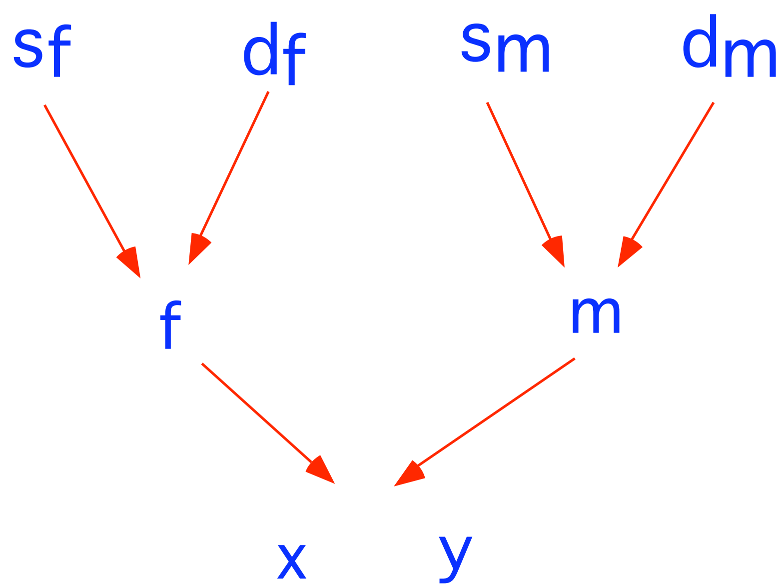
to $\Theta = (2+f_m+f_f)/8$

This gives $\Theta = (2+f_m+f_f+4\,\Theta_{mf})/8$

Full sibs (x and y) from parents m and f

$$\Theta_{xy} = (2 + f_m + f_f + 4\Theta_{mf})/8$$

$f_f = \Theta_{sf,df}$



$f_m = \Theta_{sm,dm}$

Putting all this together gives

$$\Theta_{xy} = (2 + \Theta_{sm,dm} + \Theta_{sf,df} + 4\Theta_{mf})/8$$

Computing θ_{xy} -- chain counting

Two components: First are paths through a single common ancestor (i) of both x and y

$$\Theta_{xy} = \sum_i \Theta_{ii} \left(\frac{1}{2}\right)^{n_i - 1} + \sum_j \sum_{j=k} \Theta_{jk} \left(\frac{1}{2}\right)^{n_{jk} - 2}$$

Coefficient of coancestry of i

n_i = Number of individuals (including x and y) in path connecting x and y through i

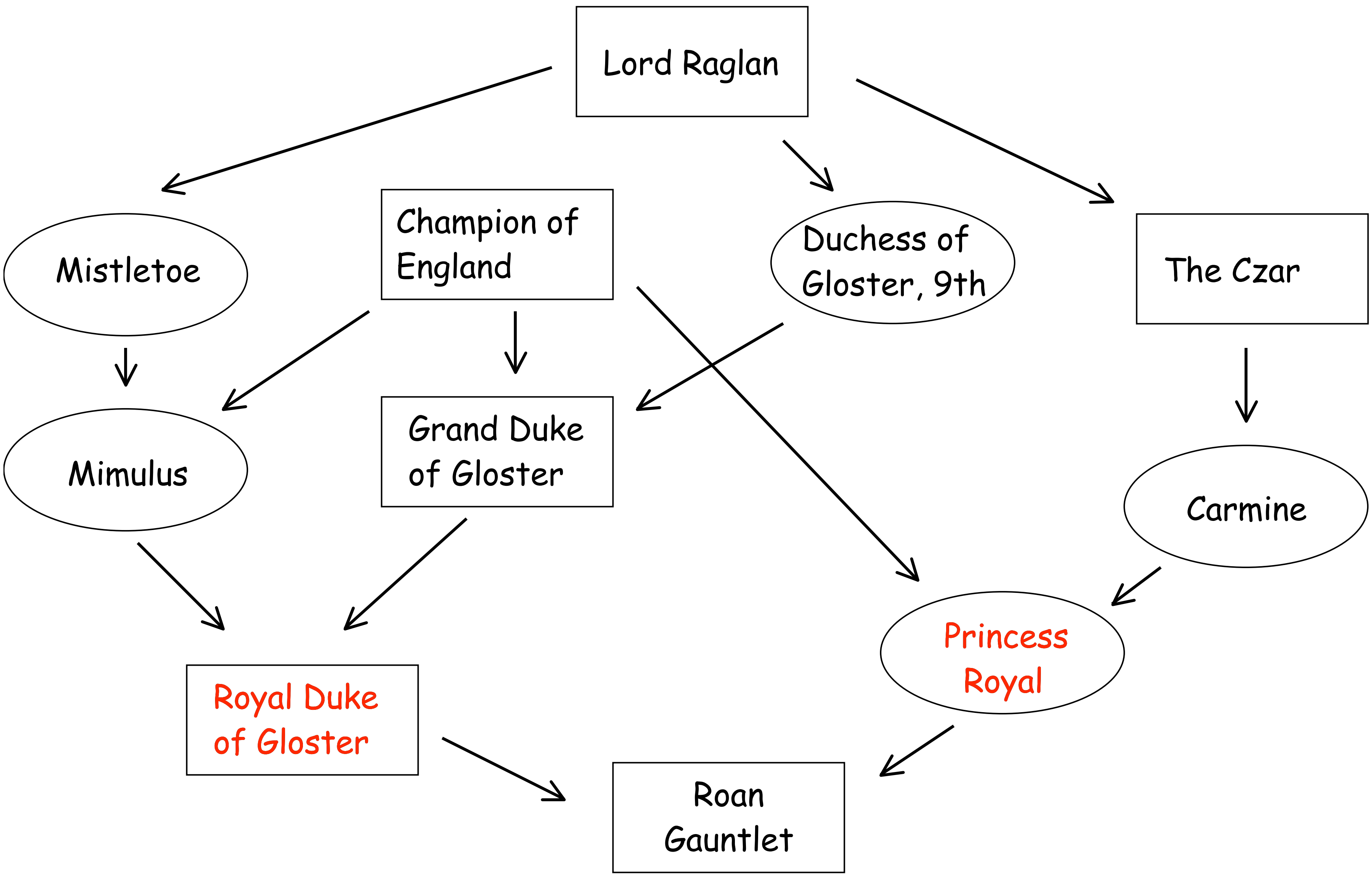
Computing θ_{xy} -- chain counting

Second component: Paths from x through j and paths from y through k, j & k related

$$\Theta_{xy} = \sum_i \Theta_{ii} \left(\frac{1}{2}\right)^{n_i - 1} + \sum_j \sum_{j=k} \Theta_{jk} \left(\frac{1}{2}\right)^{n_{jk} - 2}$$

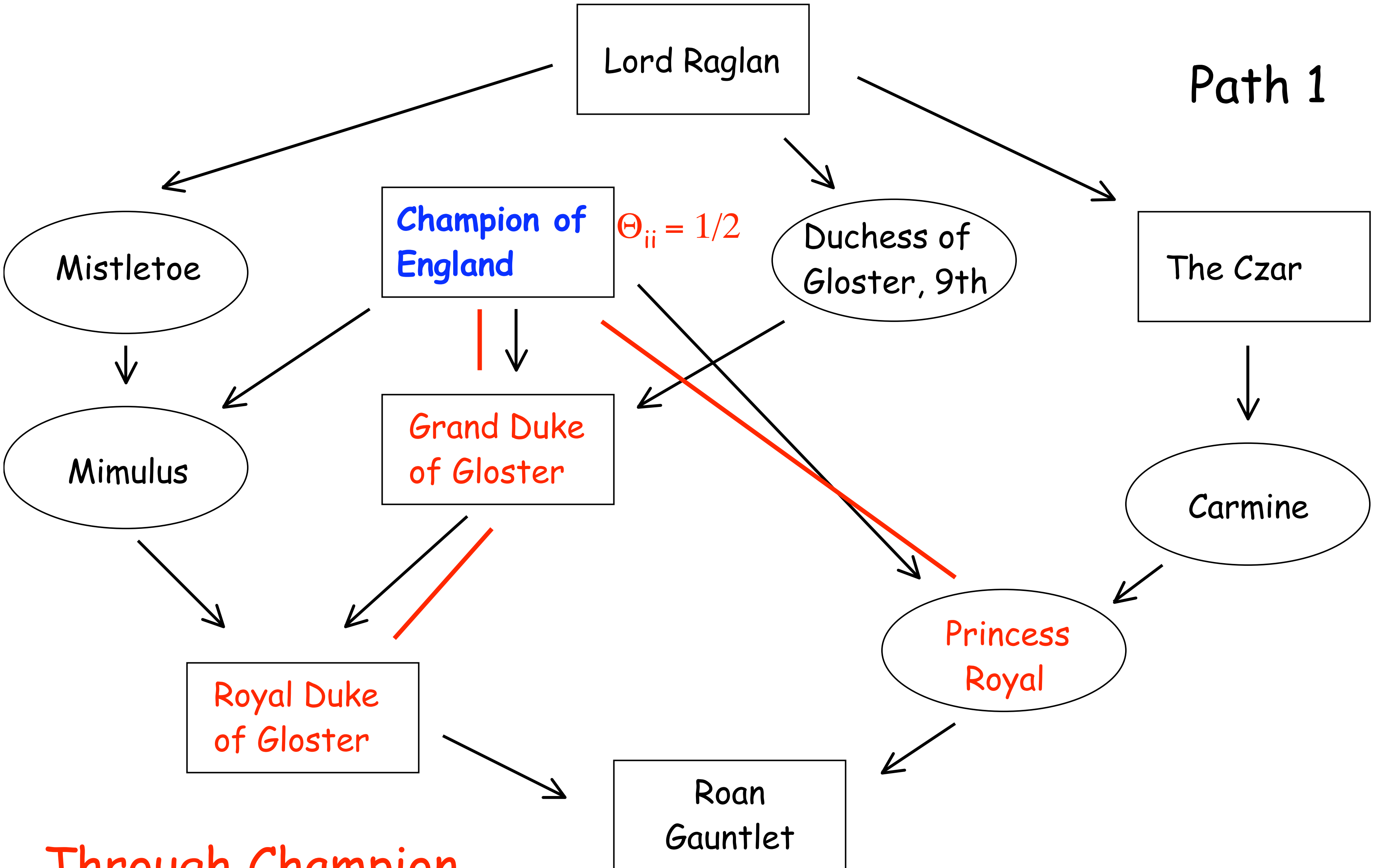
Coefficient of coancestry of j and k

Number of individuals, including x and y on the path leading from two different (but related) ancestors j and k



Compute θ for Royal Duke of Gloster and Princess Royal

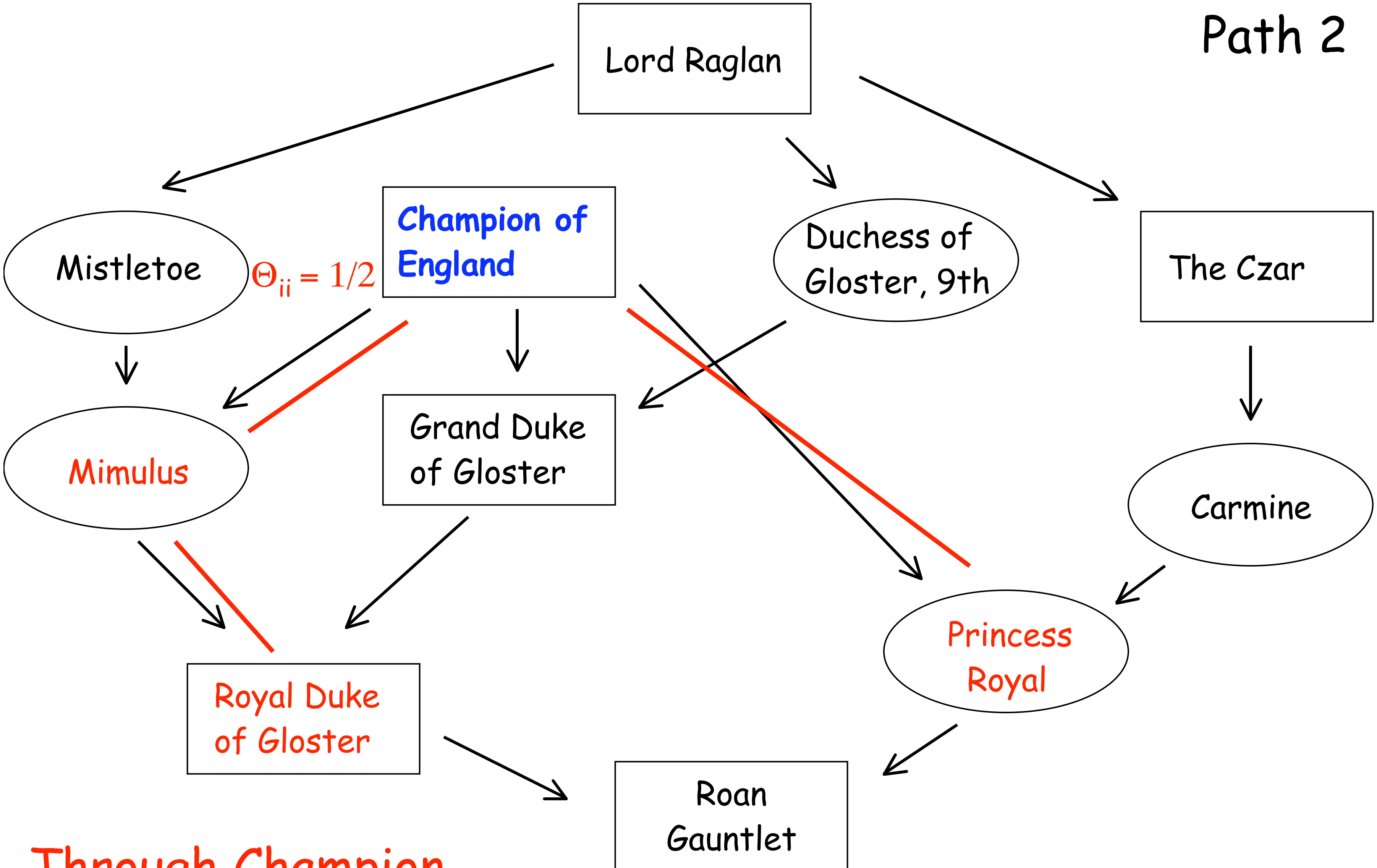
Path 1



Through Champion of England, n = 4

contribution = $(1/2)(1/2)^3$

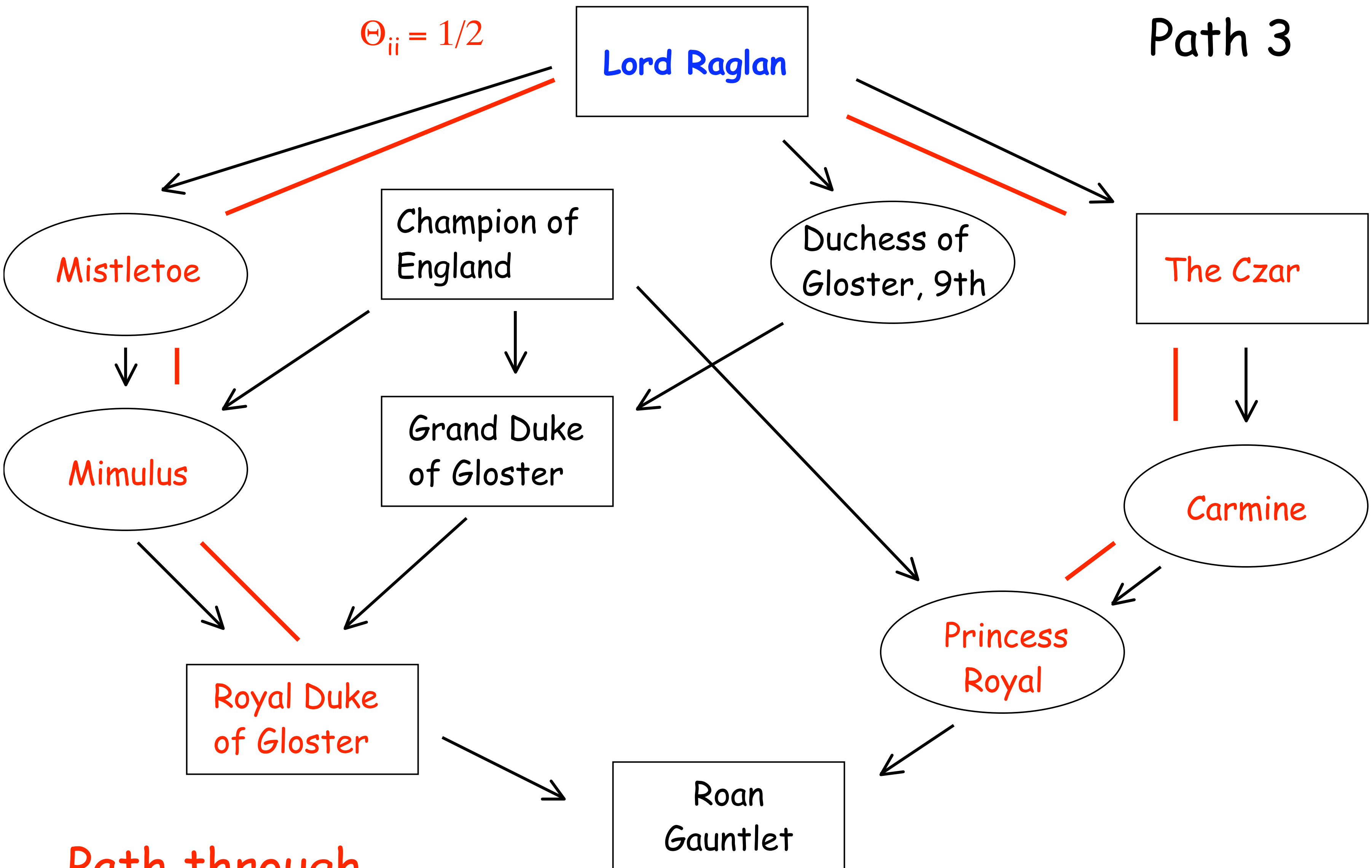
Path 2



Through Champion of England, $n = 4$

Contribution = $(1/2)(1/2)^3$

Path 3

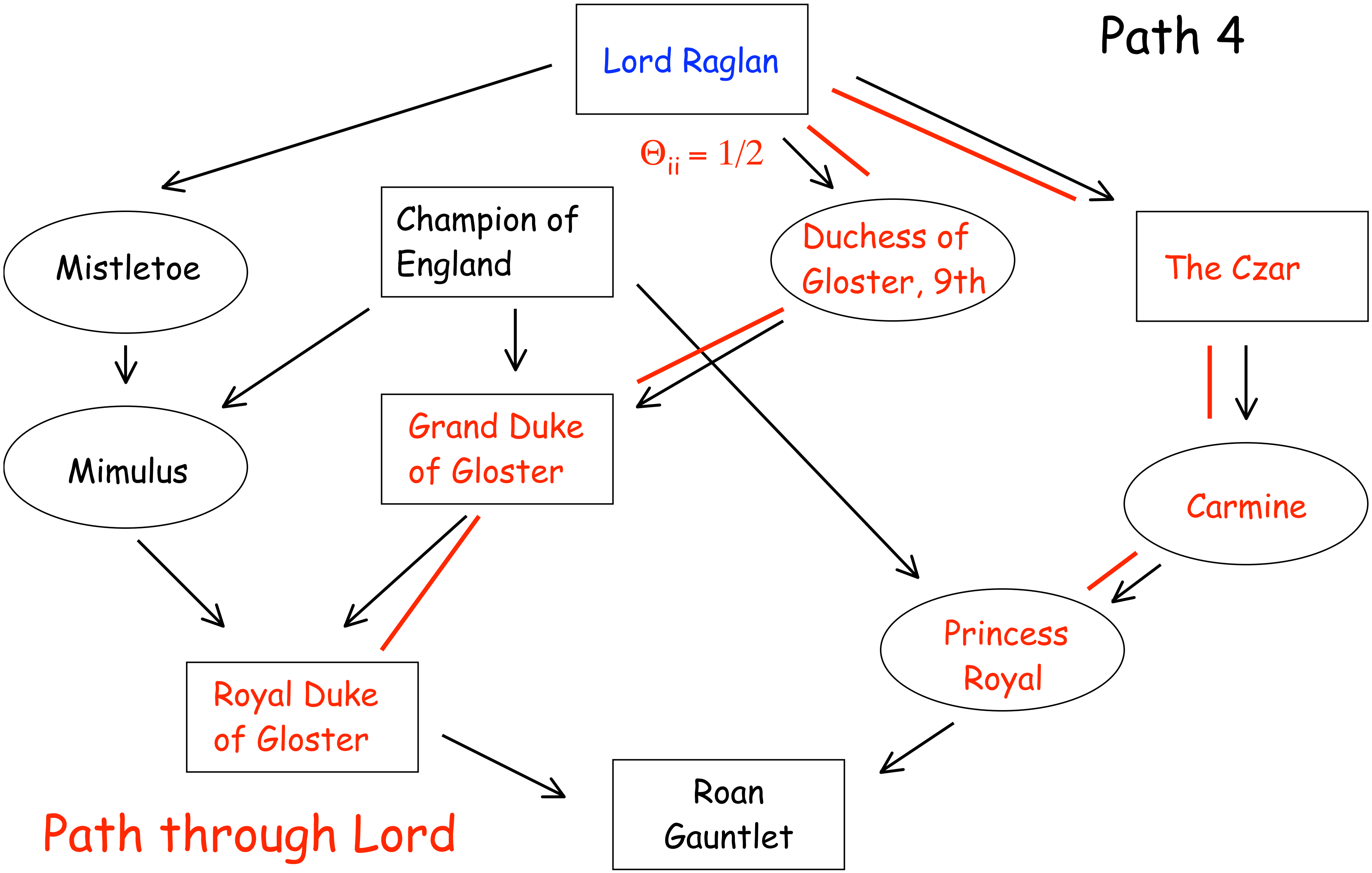


Path through

Lord Raglan, $n = 7$

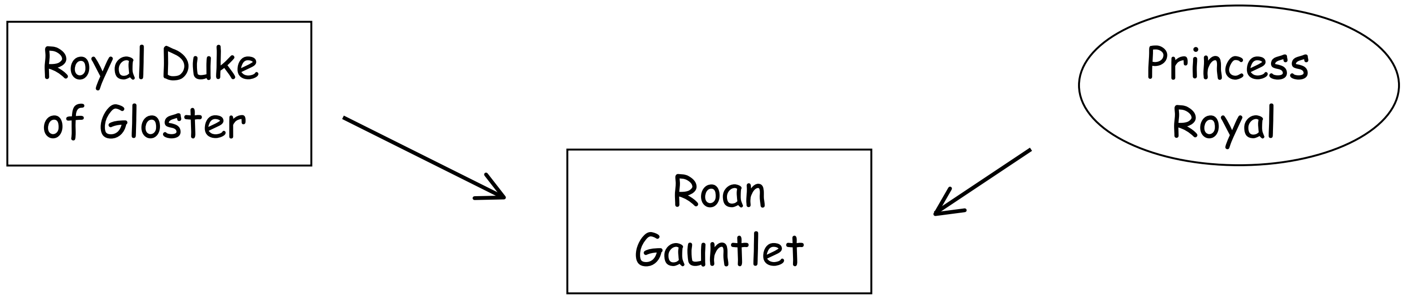
Contribution $= (1/2)(1/2)^6$

Path 4



Path through Lord Raglan, $n = 7$

Contribution = $(1/2)(1/2)^6$



Four distinct paths:

Path 1: $(1/2)^4$

Path 2: $(1/2)^4$

Path 3: $(1/2)^7$

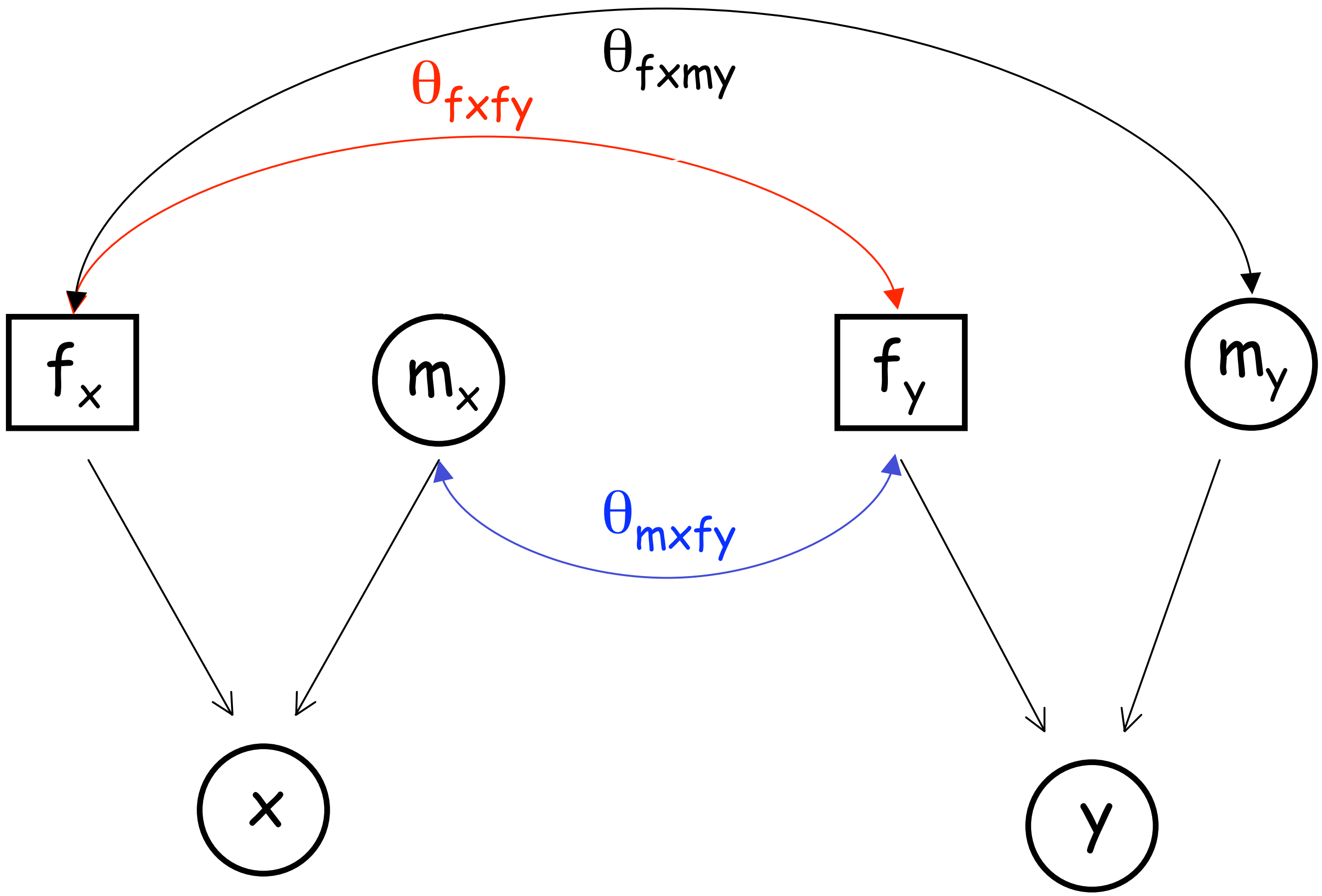
Path 4: $(1/2)^7$

total: 0.141

f for Roan Gauntlet = 0.141

Δ_{xy}, The Coefficient of Fraternity

Δ_{xy} = Prob(both alleles in x & y IBD)



$$\Delta_{xy} = \theta_{mxmy}\theta_{fxfy} + \theta_{mxfy}\theta_{fxmy}$$

Examples of Δ_{xy}

$$\Delta_{xy} = \theta_{mxmy}\theta_{fxfy} + \theta_{mxfy}\theta_{fxmy}$$

(1) x and y are full sibs: $m_x = m_y = m$, $f_x = f_y = f$

$$\Delta_{xy} = \theta_{mm}\theta_{ff} + \theta_{mf}^2$$

If parents unrelated, $\theta_{mf} = 0$

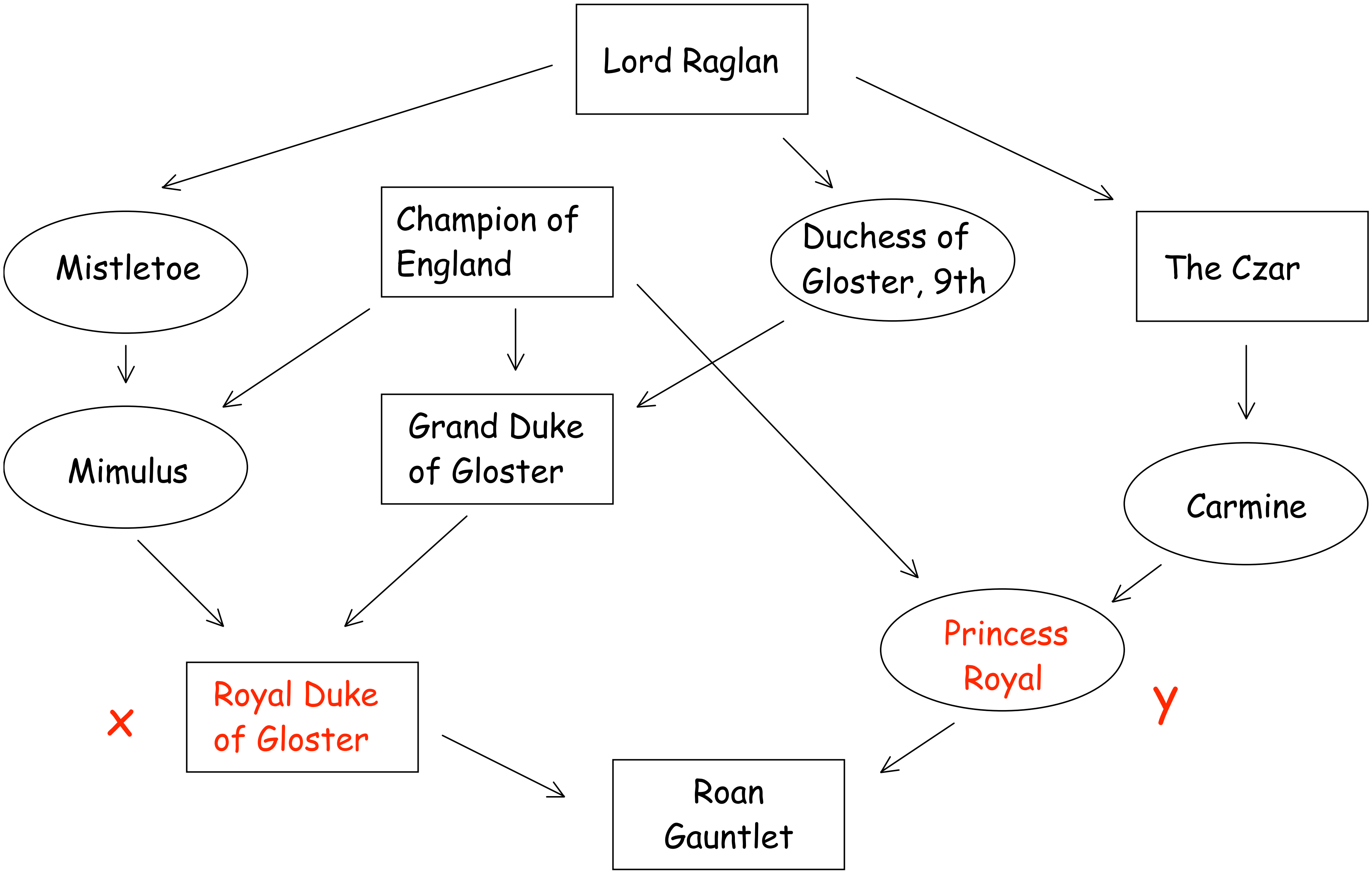
If parents not inbred, $\theta_{mm} = \theta_{ff} = 1/2$

$\Delta_{xy} = 1/4$

(2) x and y are paternal half-sibs: $f_x = f_y = f$

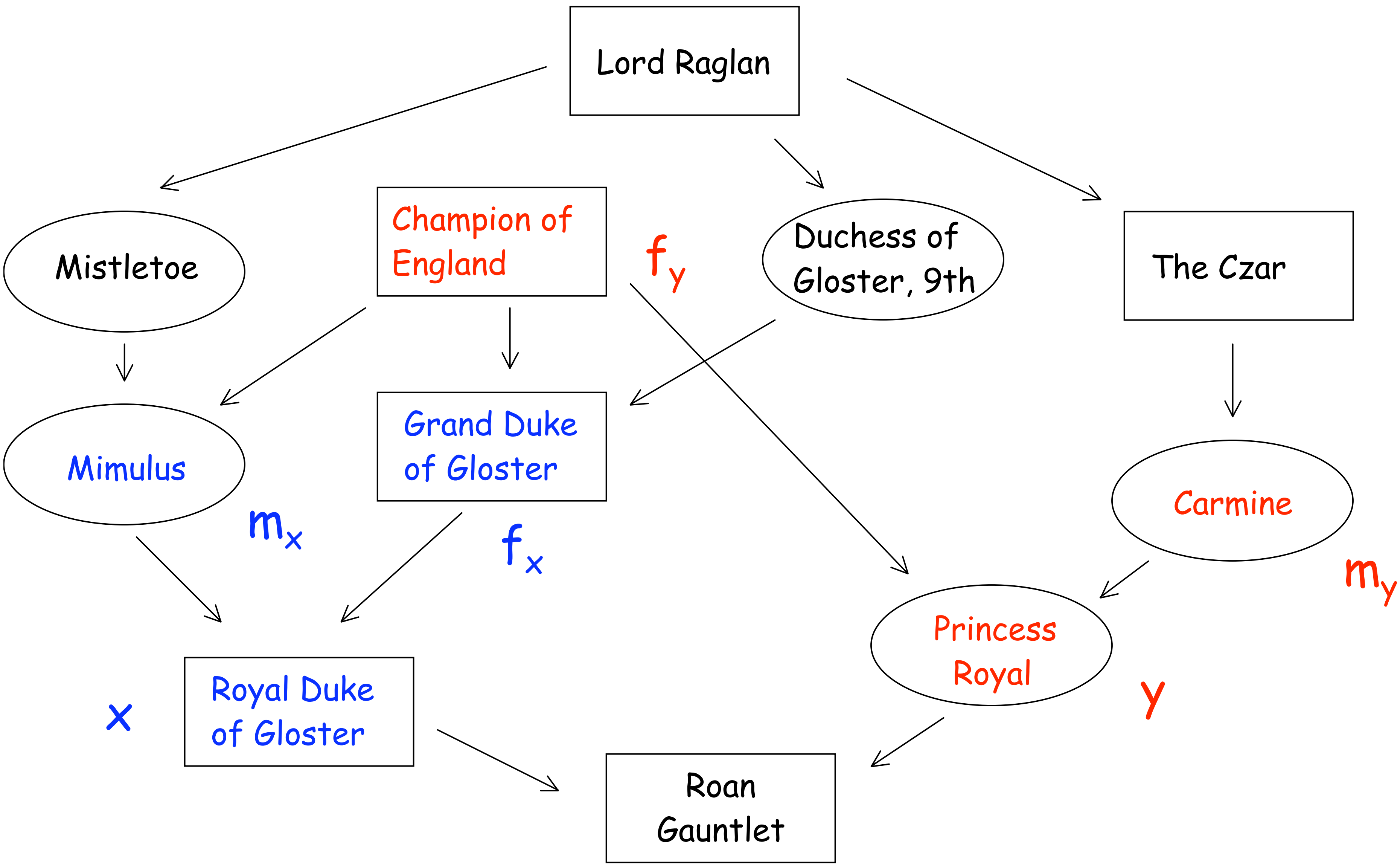
$$\Delta_{xy} = \theta_{mxmy}\theta_{ff} + \theta_{mxf}\theta_{myf}$$

If parents unrelated, $\theta_{mxf} = \theta_{myf} = \theta_{mxmy} = 0$ $\Delta_{xy} = 0$



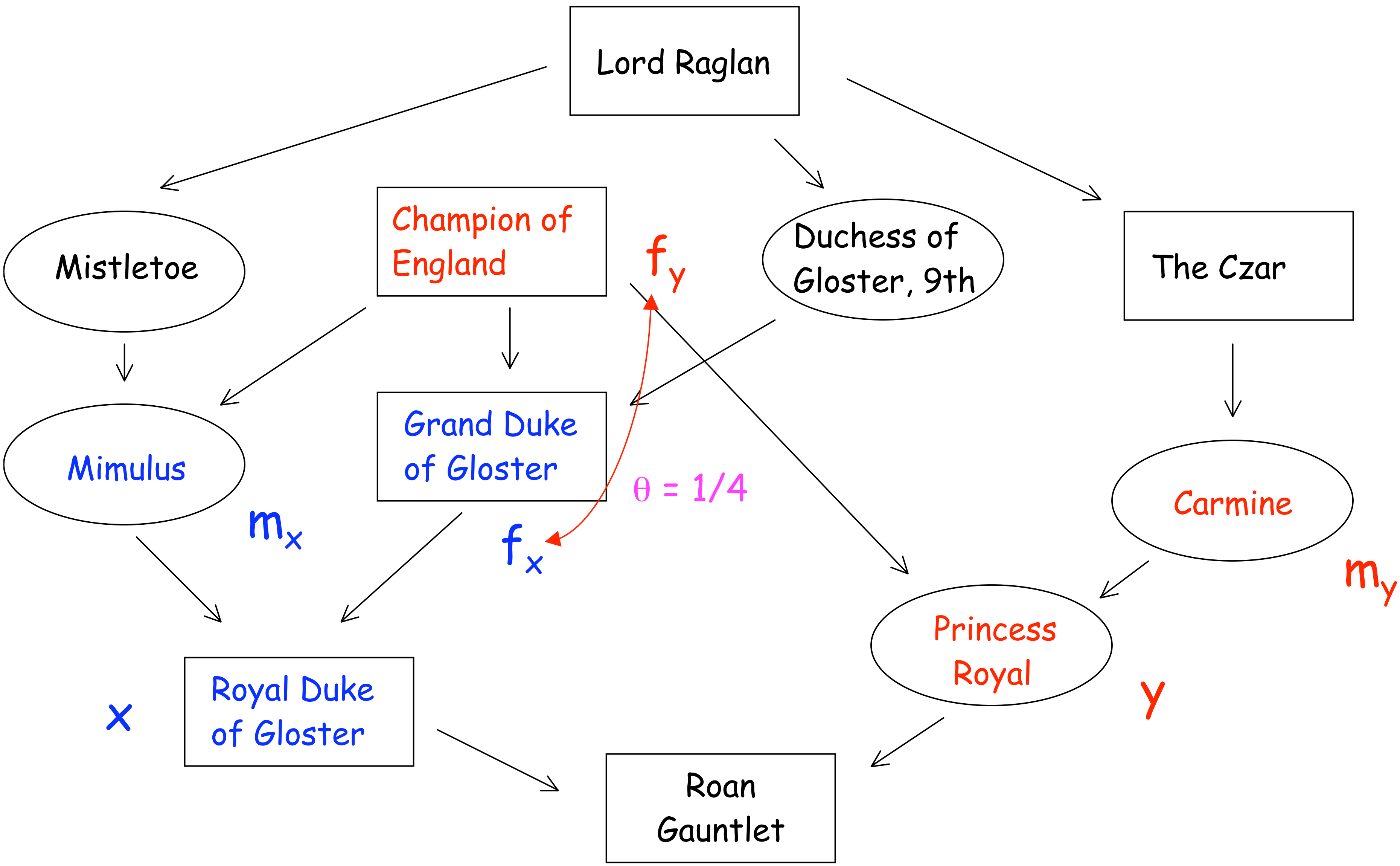
What is Δ for Royal Duke of Gloster and Princess Royal?

$$\Delta_{xy} = \theta_{mxmy}\theta_{fxfy} + \theta_{mxfy}\theta_{fxmy}$$



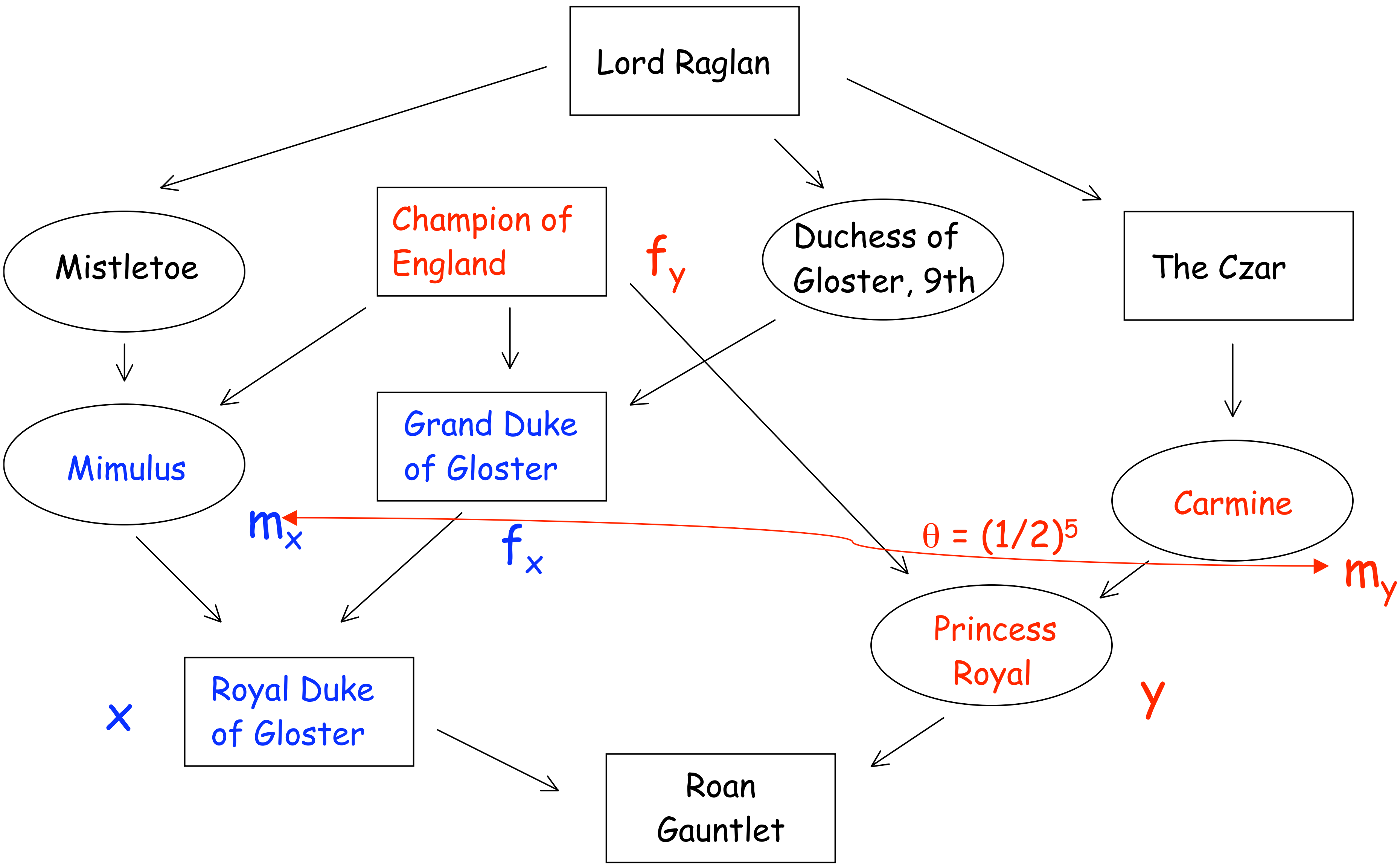
What is Δ for Royal Duke of Gloster and Princess Royal

$$\Delta_{xy} = \theta_{mxmy}\theta_{fxfy} + \theta_{mxfy}\theta_{fxmy}$$



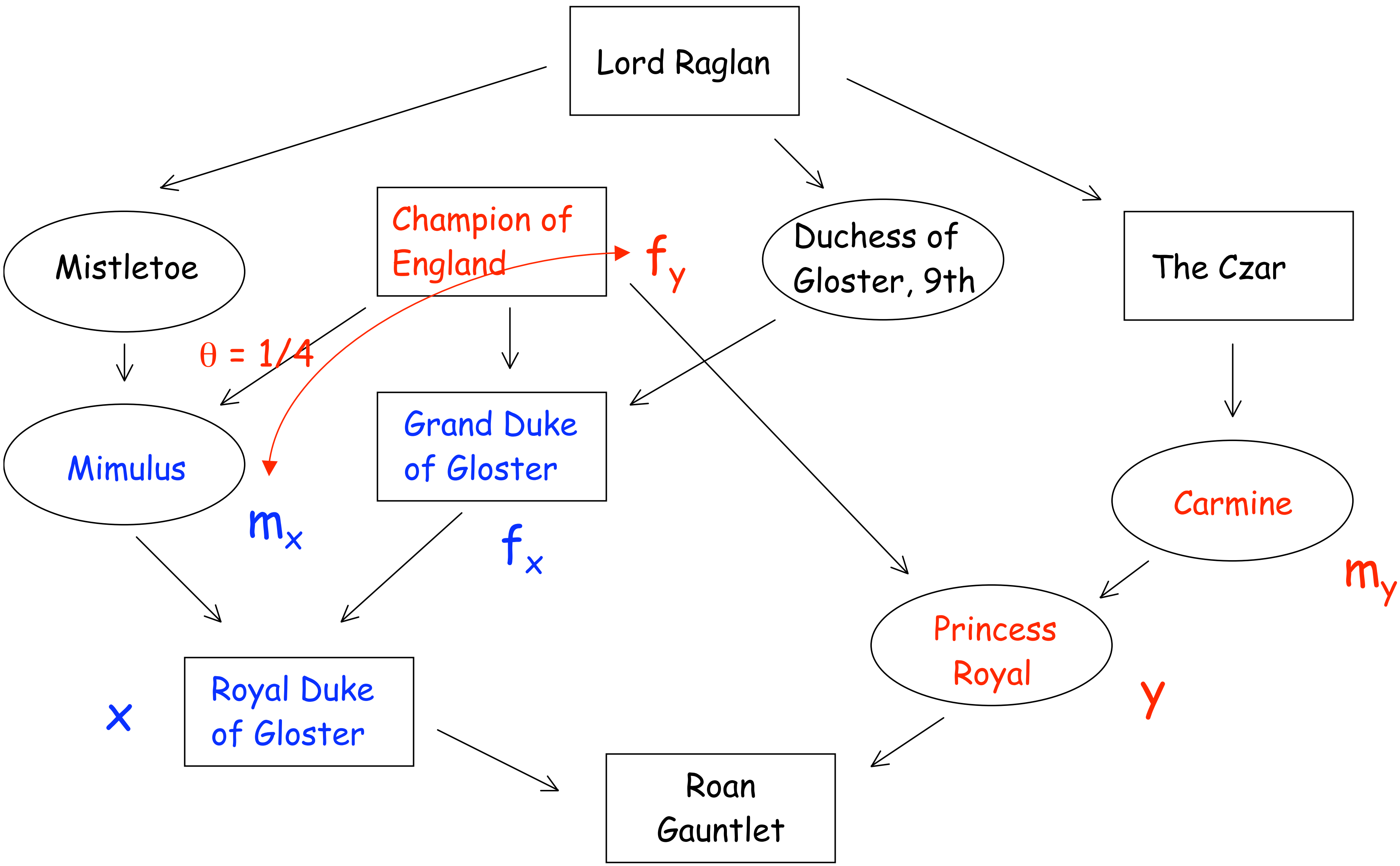
What is Δ for Royal Duke of Gloster and Princess Royal

$$\Delta_{xy} = \theta_{mxmy}(1/4) + \theta_{mxfy}\theta_{fxmy}$$



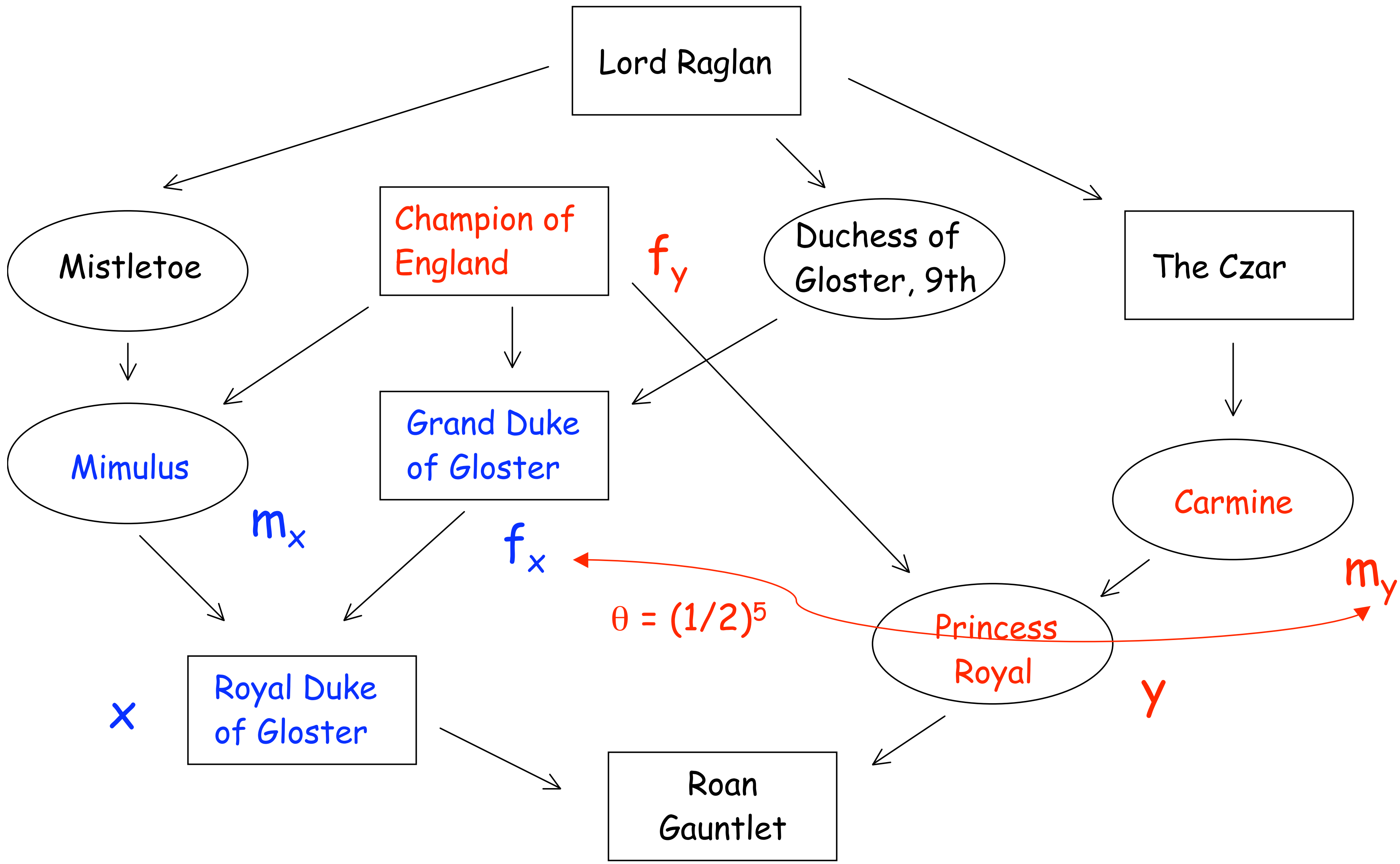
What is Δ for Royal Duke of Gloster and Princess Royal

$$\Delta_{xy} = (1/2)^5(1/4) + \theta_{mxfy}\theta_{fxmy}$$



What is Δ for Royal Duke of Gloster and Princess Royal

$$\Delta_{xy} = (1/2)^5(1/4) + (1/4)\theta_{fxmy}$$



What is Δ for Royal Duke of Gloster and Princess Royal

$$\Delta_{xy} = (1/2)^5(1/4) + (1/4)\,(1/2)^5 = (1/2)^6$$

General Resemblance between relatives

$$2\theta_{xy} = r_{xy}, \qquad u_{xy} = \Delta_{xy}$$

$$Cov(G_x, G_y) = 2\theta_{xy} V_A + \Delta_{xy} V_D$$

$$\begin{aligned} Cov(G_x, G_y) &= 2\theta_{xy} V_A + \Delta_{xy} V_D \\ &+ (2\theta_{xy})^2 V_{AA} + 2\theta_{xy} \Delta_{xy} V_{AD} + \Delta_{xy}^2 V_{DD} + \cdots \end{aligned}$$