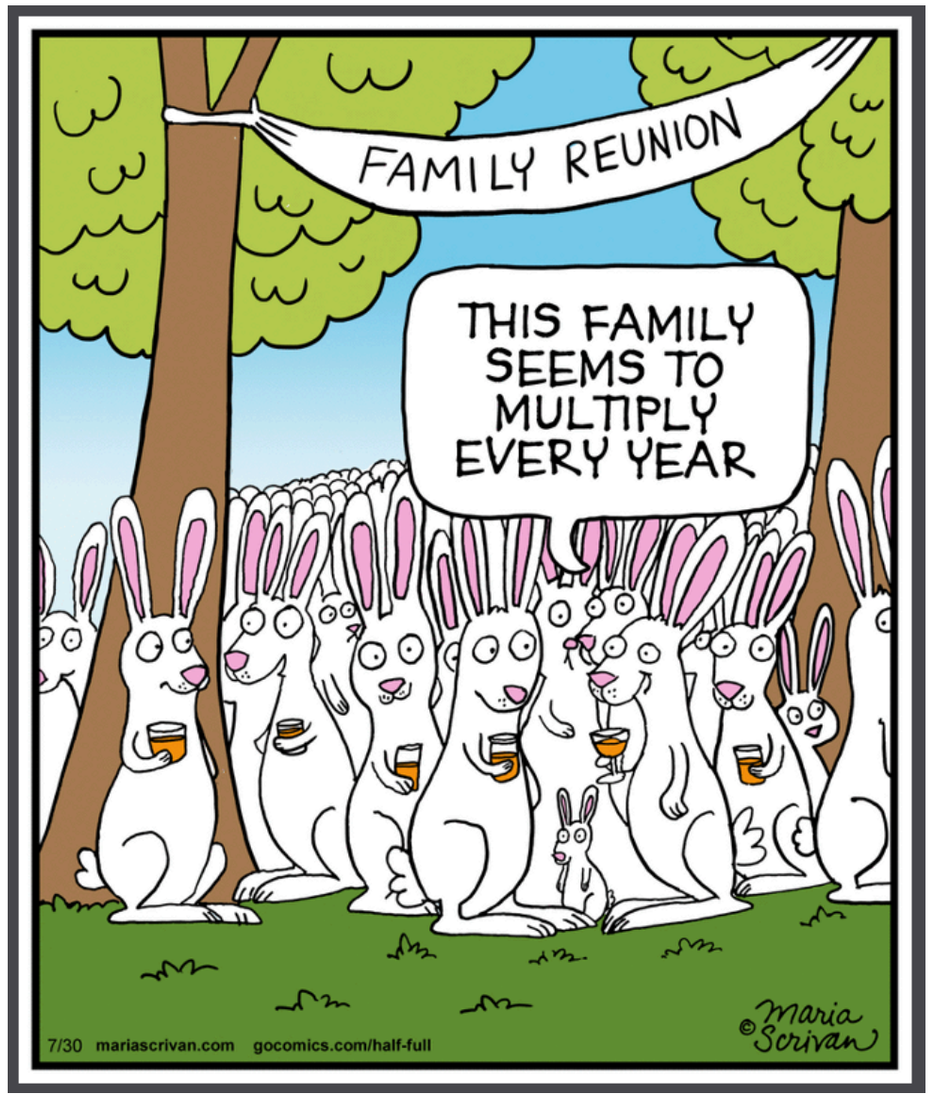
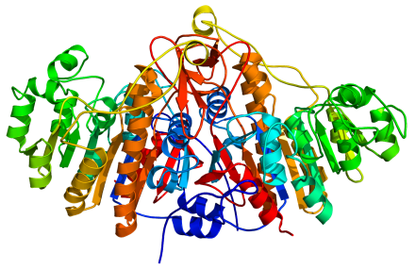
Evolutionary Genetics

LV 25600-01 | Lecture with exercises | 4KP



Non-Random Mating



Geographic variation in the allele frequency of the alkaline phosphatase (ALP) in humans.
Source: Roychoudhury and Nei 1988

	freq(S)	freq(F)	freq(I)	others	n
England	0.637	0.270	0.085	0.008	597
Italy	0.661	0.256	0.075	0.007	273
West India	0.701	0.217	0.066	0.016	208
Thailand	0.746	0.081	0.165	0.008	188
Japan	0.724	0.038	0.236	0.003	294
Nigeria	0.942	0.019	0.039	0.000	130
Canadian Inuits	0.556	0.142	0.296	0.006	81
Papua New Guinea	0.881	0.050	0.068	0.002	338
Total					2109

Can you explain the observed patterns of geographical variation in ALP alleles among human populations?

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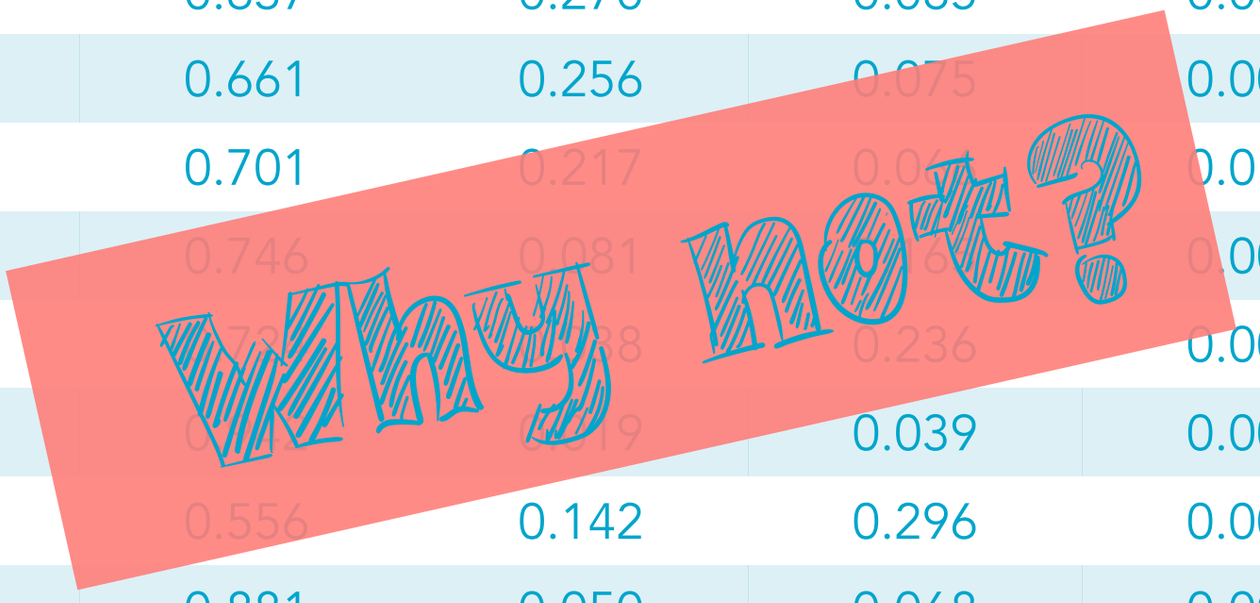


The human population is **not** one large **randomly mating** population.

A combination of cultural, social, historical, and environmental factors has shaped the distribution of the human population into different subpopulations with distinct genetic characteristics. While globalisation and increased mobility have led to greater mixing of populations, the effects of historical isolation and cultural practices still influence human genetic diversity.

Human genetic diversity has been shaped by a complex interplay of cultural, social, historical and environmental factors, each of which influences the distribution of genetic traits across populations. For example, early human migrations were often driven by environmental pressures such as climate change and resource availability, resulting in geographically dispersed populations that adapted to local conditions over thousands of years. Historical periods of isolation due to geographical barriers, such as mountain ranges or oceans, further contributed to genetic differentiation as these groups evolved largely independently.

Social and cultural practices, including language, religion and marriage customs, have also historically limited gene flow between populations, reinforcing genetic differences. In some cases, these practices have resulted in unique genetic signatures within certain populations due to endogamy (marriage within a particular group) and other forms of cultural isolation.

While recent globalisation and increased human mobility have facilitated greater genetic mixing between populations, creating a more interconnected gene pool, the effects of historical isolation and cultural practices still persist. These patterns are evident in the genetic predispositions, adaptations and health traits observed in different human populations today, reflecting both the ancient forces that shaped early populations and the ongoing dynamics of our interconnected world.

PopGen ▷ Non-Random Mating

The human population is not one large randomly mating population due to several factors:

Geographic barriers - Historically, people have been separated by geographical features such as mountains, deserts, rivers and oceans. These physical barriers limit the movement of people and contribute to the formation of isolated populations. Over time, these isolated populations can develop genetic differences (e.g. genetic drift, limited gene flow).

Cultural preferences - Cultural practices, including mate choice and marriage customs, play an important role in shaping human populations. Many cultures have specific rules and preferences regarding marriage partners, often based on factors such as religion, ethnicity or social class. These cultural preferences can lead to the formation of distinct groups with limited interbreeding.

Social structures - Human societies often have social structures that influence mating patterns. For example, caste systems, social classes and other hierarchical structures can influence mate choice and restrict gene flow between different social groups.

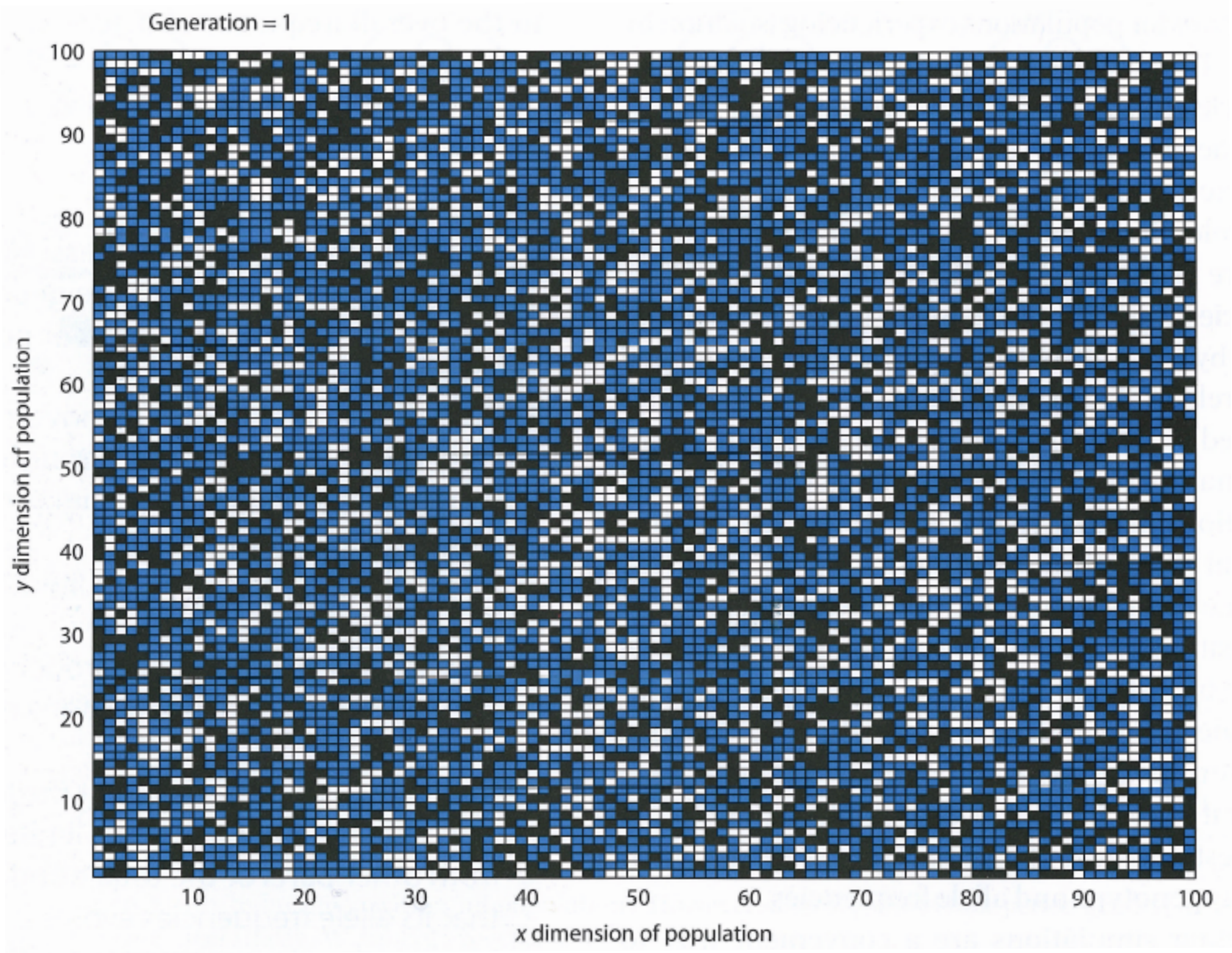
Historical migrations - Throughout history, human populations have migrated for a variety of reasons, including environmental changes, economic opportunities, or fleeing conflict. These migrations have led to the mixing of populations, but have also contributed to the formation of regional genetic variation.

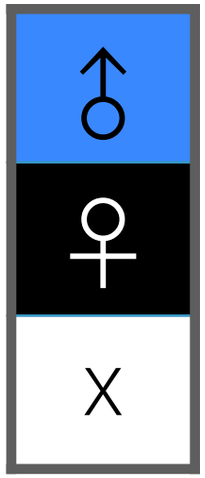
Evolutionary history - Over thousands of years, human populations have adapted to their local environments. This has led to the development of specific genetic traits that are advantageous in those environments. These adaptations can contribute to genetic differences between populations.

Natural selection - Environmental factors such as climate, altitude and disease prevalence can influence natural selection. Populations living in different environments may develop adaptations specific to those conditions, further contributing to genetic diversity.

Cultural and economic globalisation - While modern transport and communications have reduced some geographical barriers, cultural and economic factors still play an important role in limiting gene flow. People often marry within their cultural or socio-economic group, even in more globally connected societies.

PopGen ▷ Non-Random Mating





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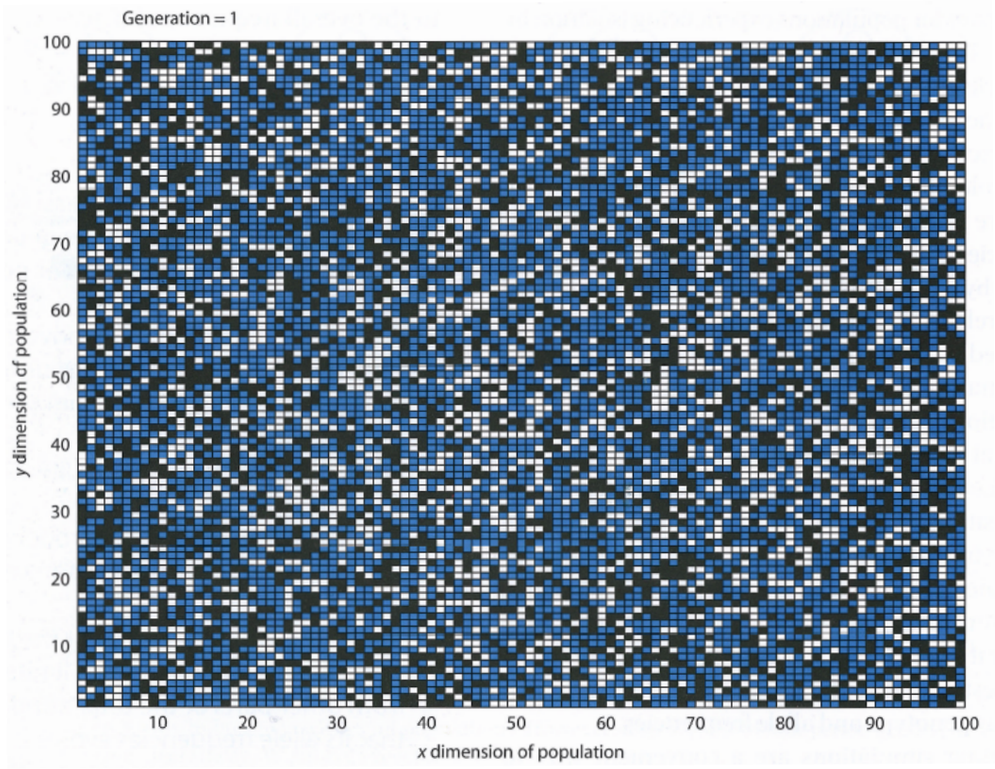
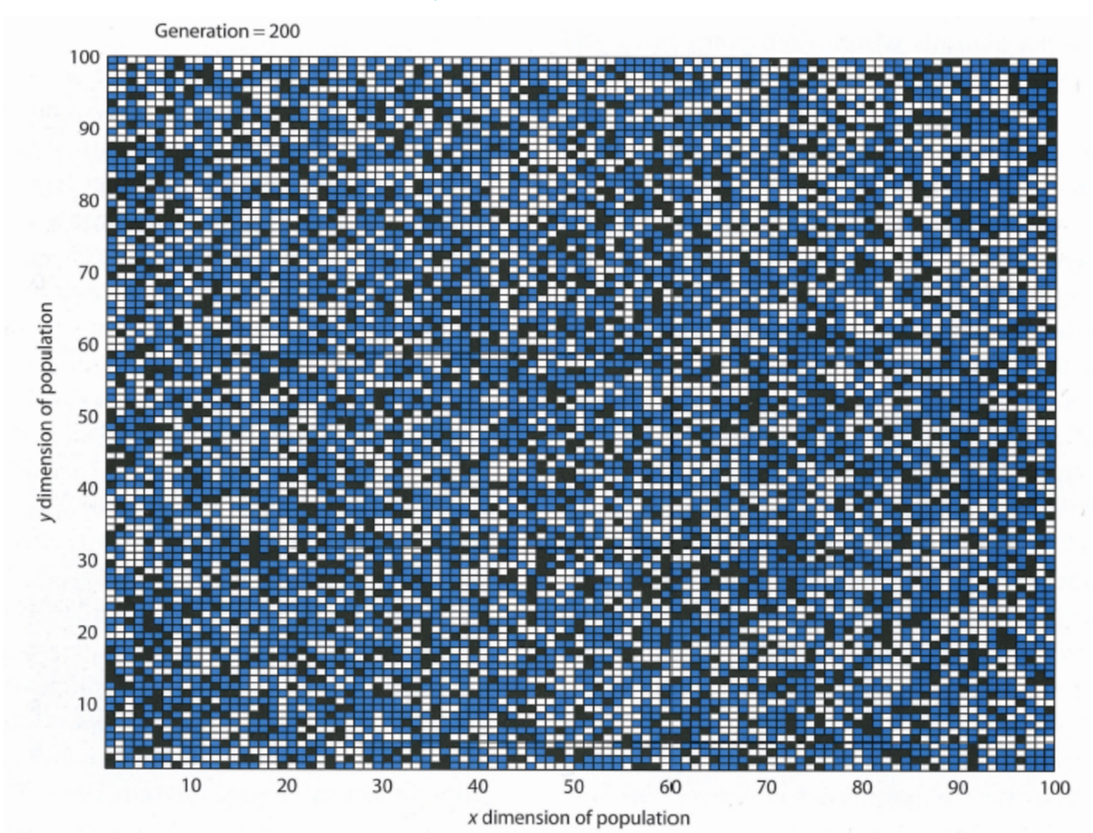


random mating

isolation by distance



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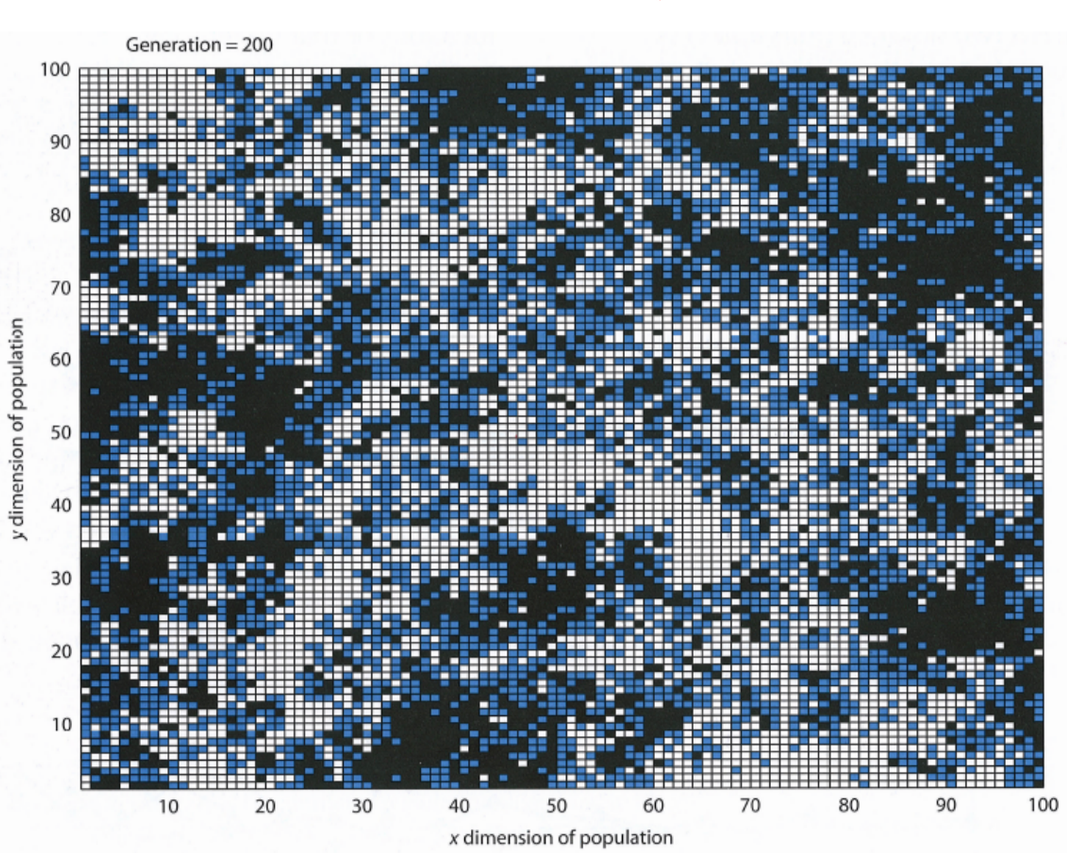

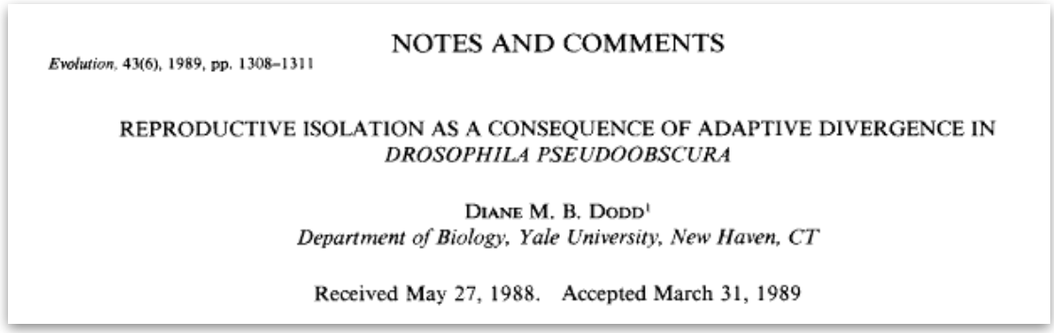

NOTES AND COMMENTS

Evolution, 43(6), 1989, pp. 1308–1311

REPRODUCTIVE ISOLATION AS A CONSEQUENCE OF ADAPTIVE DIVERGENCE IN *DROSOPHILA PSEUDOOBSCURA*

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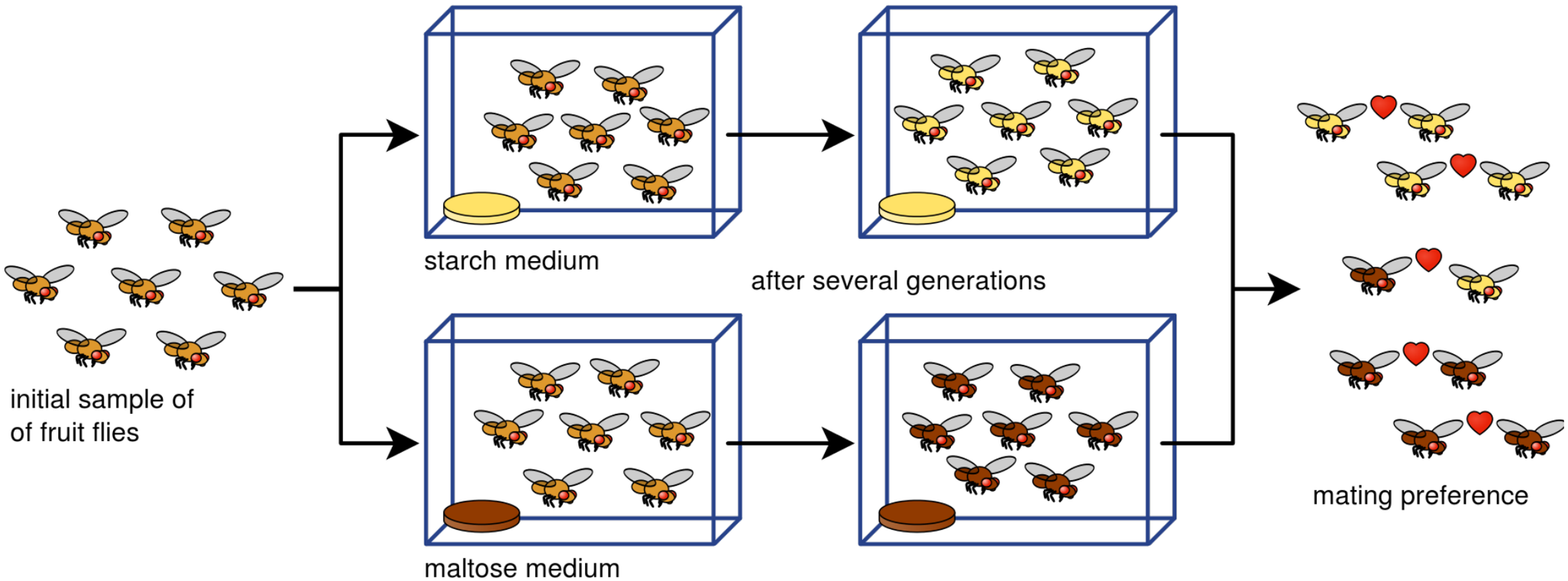
Department of Biology, Yale University, New Haven, CT

Received May 27, 1988. Accepted March 31, 1989



In 1989 Diane Dodd gave laboratory populations of *D. pseudoobscura* two different food types, starch and maltose. They rapidly evolved into two distinct groups after only eight generations with the different foods. As the two groups both showed a **strong preference for mating with their own type**, this was claimed as an example of **speciation by reproductive isolation**.

Non-Random Mating

Non-random mating occurs when the probability that two individuals in a population will mate is not the same for all possible pairs of individuals. If the probability is the same for all possible pairs, it is considered to be random mating.

Assortative Mating

Mating patterns in which individuals with **similar traits or characteristics** are more likely to choose each other as mates. This can lead to an increase in the similarity of these traits within a population.

Disassortative Mating

(Negativ Assortative)

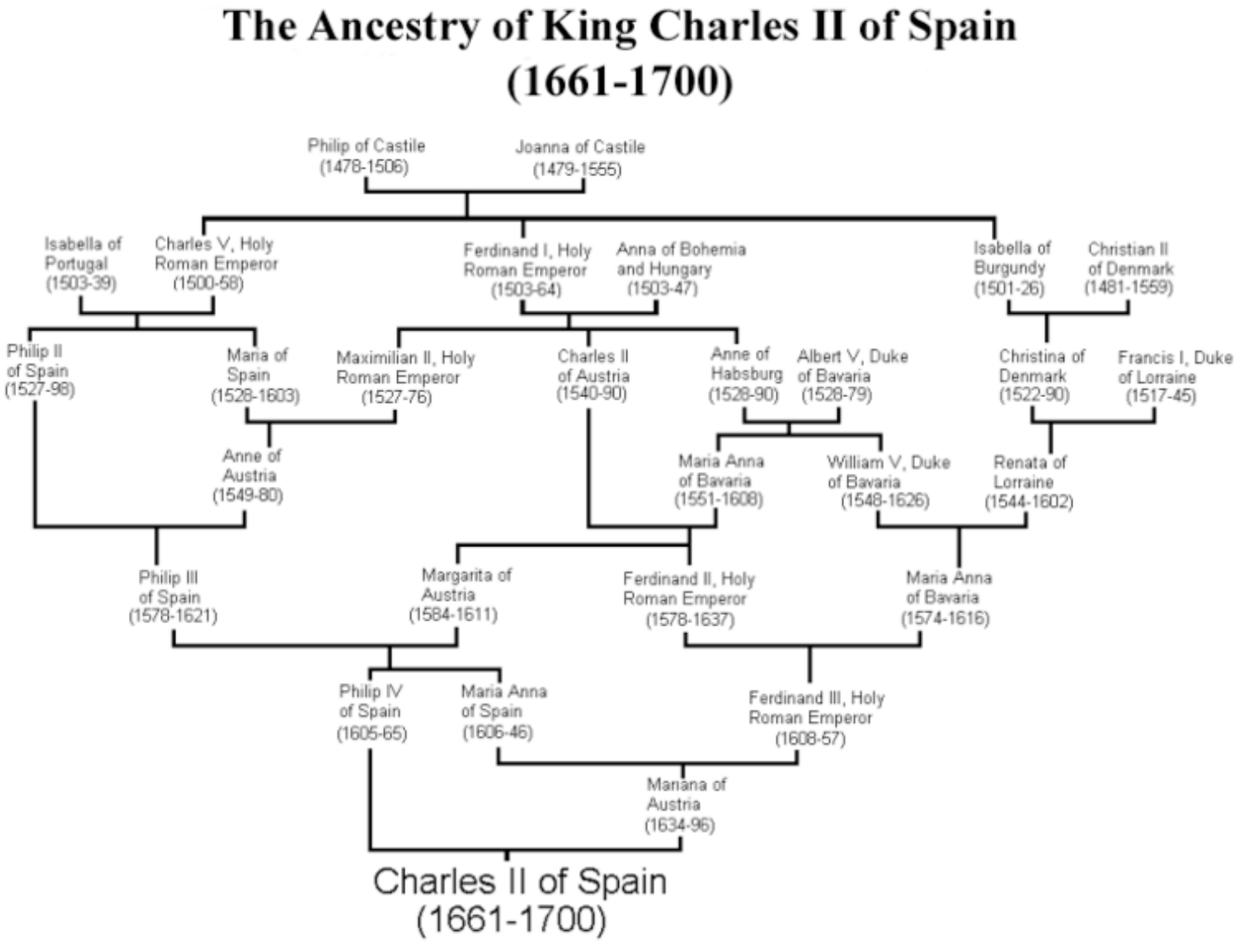
In contrast to assortative mating, it promotes diversity by favouring the mating of individuals with contrasting traits. This can help avoid inbreeding because individuals with different traits are less genetically related to each other. It can also help maintain a broader gene pool, which can be beneficial for the long-term health of a population by preventing genetic homogeneity.

Inbreeding

Inbreeding is the mating of individuals **related by ancestry**. The consequence of mating with a relative is that offspring have an increased probability of inheriting alleles that are recent copies of the same allele (i.e. identical by descent, or autozygous).

Inbreeding - Recessive Deleterious Mutations

Charles II of Spain, known as 'The Enchanted' or 'El Hechizado', was born on 6 November 1661 and reigned as King of Spain from 1665 until his death in 1700. He was the last Habsburg ruler of Spain and his life was marked by significant physical and mental health challenges. Charles's reign is often associated with the decline of the Spanish Habsburg dynasty and the weakening of the Spanish Empire. His parents, Philip IV of Spain and his second wife, Mariana of Austria, were closely related - the result of extensive intermarriage among European royalty. This inbreeding contributed to Charles's severe physical and mental disabilities, including a pronounced underbite, a large tongue and a frail constitution.


The Ancestry of King Charles II of Spain
(1661-1700)
Philip of Castile
(1478-1506)
Joanna of Castile
(1479-1555)
Isabella of Portugal (1503-39)
Charles V, Holy Roman Emperor (1500-58)
Ferdinand I, Holy Roman Emperor (1503-64)
Anna of Bohemia and Hungary (1503-47)
Isabella of Burgundy (1501-26)
Christian II of Denmark (1481-1559)
Philip II of Spain (1527-98)
Maria of Spain (1528-1603)
Maximilian II, Holy Roman Emperor (1527-76)
Charles II of Austria (1540-90)
Anne of Habsburg (1528-90)
Albert V, Duke of Bavaria (1528-79)
Christina of Denmark (1522-90)
Francis I, Duke of Lorraine (1517-45)
Anne of Austria (1549-80)
Maria Anna of Bavaria (1551-1608)
William V, Duke of Bavaria (1548-1626)
Renata of Lorraine (1544-1602)
Philip III of Spain (1578-1621)
Margarita of Austria (1584-1611)
Ferdinand II, Holy Roman Emperor (1578-1637)
Maria Anna of Bavaria (1574-1616)
Philip IV of Spain (1605-65)
Maria Anna of Spain (1606-46)
Ferdinand III, Holy Roman Emperor (1608-57)
Mariana of Austria (1634-96)
Charles II of Spain
(1661-1700)

Nature Reviews Genetics 10, 783-796 (November 2009) | doi:10.1038/nrg2664

The genetics of inbreeding depression

Charlesworth D and Willis JH

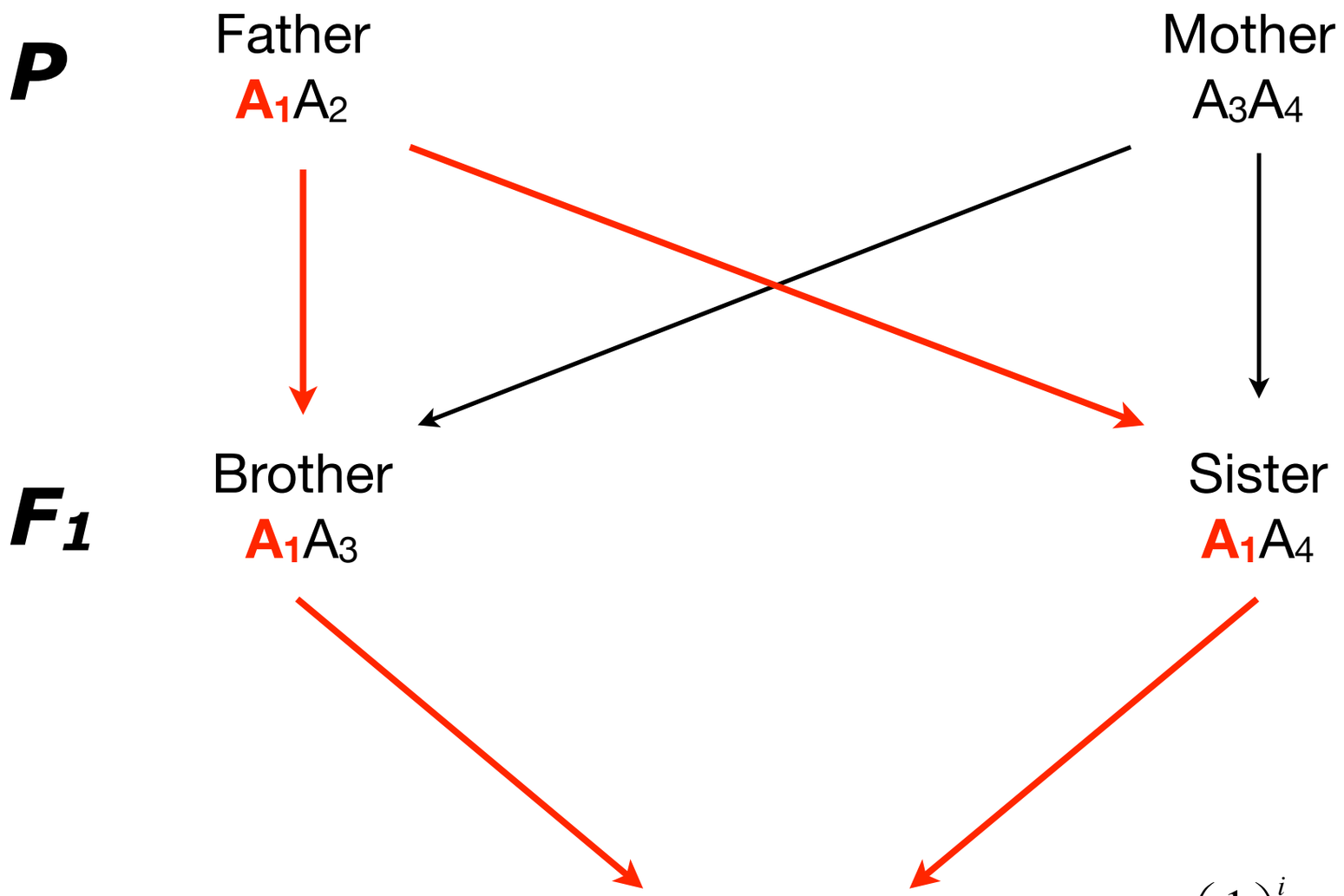
Inbreeding depression — the **reduced survival and fertility of offspring of related individuals** — occurs in wild animal and plant populations as well as in humans, indicating that **genetic variation in fitness traits** exists in natural populations. Inbreeding depression is important in the evolution of outcrossing mating systems and, because intercrossing inbred strains improves yield (heterosis), which is important in crop breeding, the genetic basis of these effects has been debated since the early twentieth century. Classical genetic studies and modern molecular evolutionary approaches now suggest that inbreeding depression and heterosis are predominantly caused by the presence of **recessive deleterious mutations in populations**.

Genetics. 2015 Apr;199(4):1243-54. doi: 10.1534/genetics.114.173351. Epub 2015 Feb 18

An estimate of the average number of recessive lethal mutations carried by humans

Z Gao, D Waggoner, M Stephens, C Ober , M Przeworski

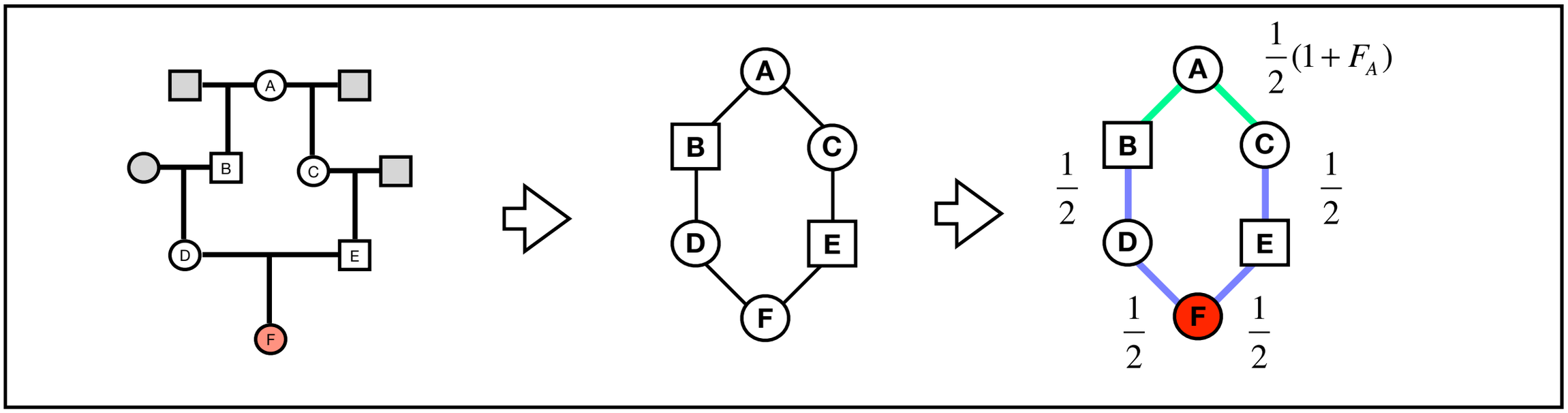
The effects of inbreeding on human health depend critically on the number and severity of recessive, deleterious mutations carried by individuals. In humans, existing estimates of these quantities are based on comparisons between consanguineous and non-consanguineous couples, an approach that confounds socioeconomic and genetic effects of inbreeding. To overcome this limitation, we focused on a founder population that practices a communal lifestyle, for which there is almost complete Mendelian disease ascertainment and a known pedigree. Focusing on recessive lethal diseases and simulating allele transmissions, we estimated that each haploid set of **human autosomes carries on average 0.29** (95% credible interval [0.10, 0.84]) **recessive alleles that lead to complete sterility or death by reproductive age when homozygous.** Comparison to existing estimates in humans suggests that a substantial fraction of the total burden imposed by recessive deleterious variants is due to single mutations that lead to sterility or death between birth and reproductive age. In turn, comparison to estimates from other eukaryotes points to a surprising constancy of the average number of recessive lethal mutations across organisms with markedly different genome sizes.



$$F_{IF} = \left(\frac{1}{2}\right)^{i}(1+F_F) \Rightarrow \left(\frac{1}{2}\right)^{3} = \frac{1}{8}$$

$$F_{IM} = \left(\frac{1}{2}\right)^{i}(1+F_M) \Rightarrow \left(\frac{1}{2}\right)^{3} = \frac{1}{8}$$

$$F_I^{total} = 25\%$$



a. Identify all **common ancestors** in the pedigree → F_A

b. Trace all the **paths of gametes** (DB<u>A</u>CE) → i

c. Calculate inbreeding coefficient → F_I

$$F_I = \left(\frac{1}{2}\right)^i (1+F_A) \overset{F_A=0}{\Rightarrow} \left(\frac{1}{2}\right)^5 = \frac{1}{32}$$

Inbreeding increases the frequency of homozygotes and reduces heterozygosity.

homozygotes ↑

heterozygotes ↓

We can use the decrease in heterozygosity due to inbreeding to measure the effect of inbreeding.

$$F = 1 - \frac{H_o}{H_e} \rightarrow 1 - \frac{H}{2pq}$$

The inbreeding coefficient of an individual (F) is the probability that an individual has two alleles at a locus that are identical by descent. It measures the amount of inbreeding by comparing the **observed** frequency of heterozygotes (H_o) in the population with the frequency expected (H_e) under random mating - Hardy-Weinberg.

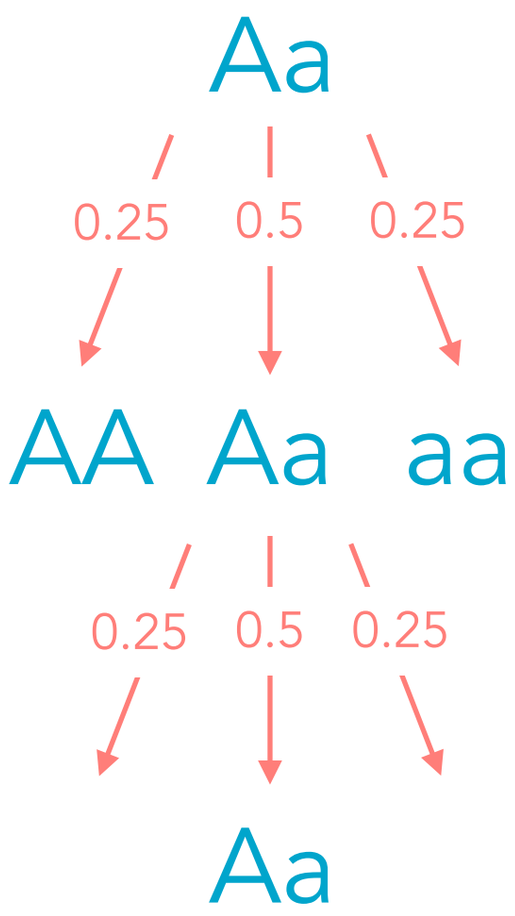
For a population in HWE, H_e is not significantly different from H_o and therefore inbreeding (*F*) would be 0.

$$F = 1 - \frac{H_o}{H_e} \xrightarrow{H_o \approx H_e} 1 - 1 = 0$$

$F : [0,1]$

$F = 0 \rightarrow$ random mating

Selfing: $F = 0.5$ (loss of 50% of total variation per generation)

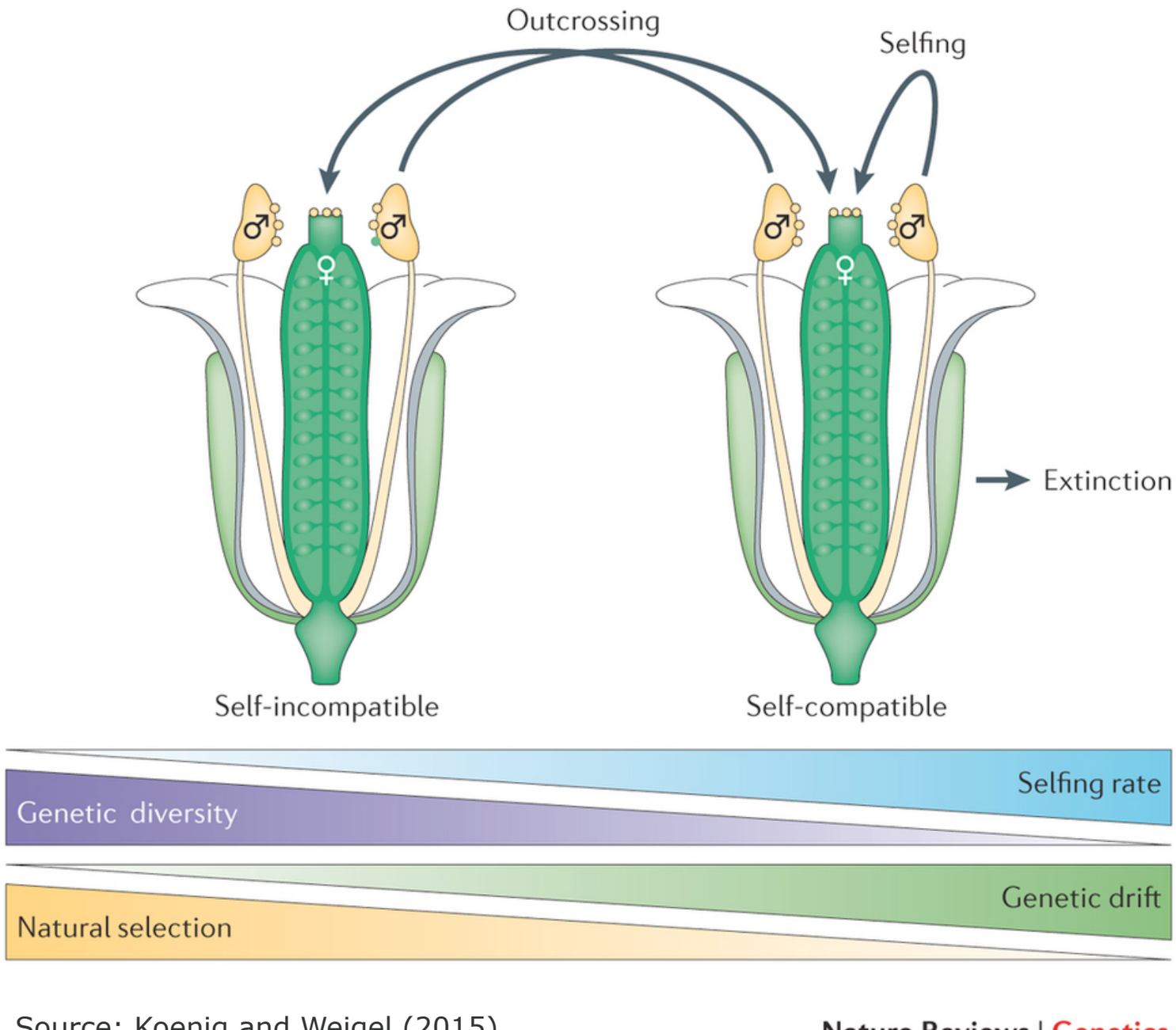


Generation	AA	Aa	aa
1	0.250	0.500	0.250
2	0.375	0.250	0.375
3	0.438	0.125	0.438
…	…	…	…
>10	0.5	0.0	0.5

Example of the effects of inbreeding

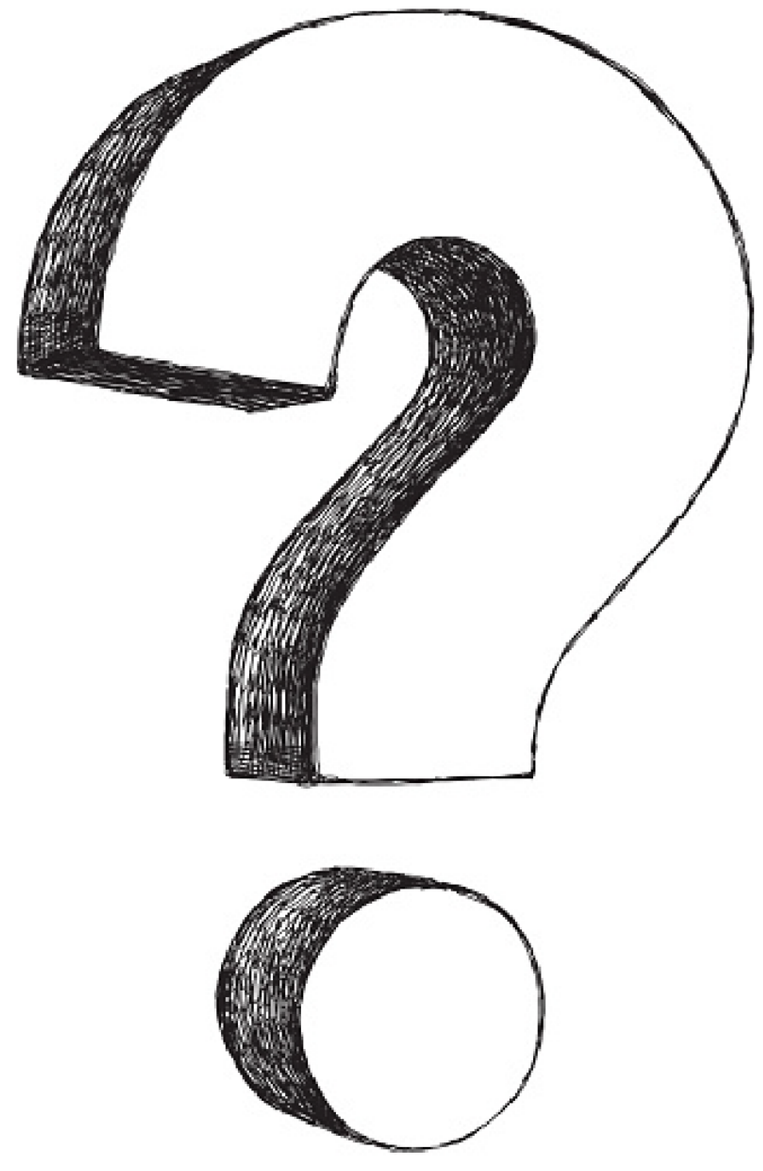
$$p = 0.6,\ q = 0.4,\ 2pq = 0.48$$

	$F = 0$	$F = 0.5$
$freq(AA) = p^2 + Fpq$	0.36	0.48
$freq(Aa) = 2pq - 2Fpq$	0.48	0.24
$freq(aa) = q^2 + Fpq$	0.16	0.28

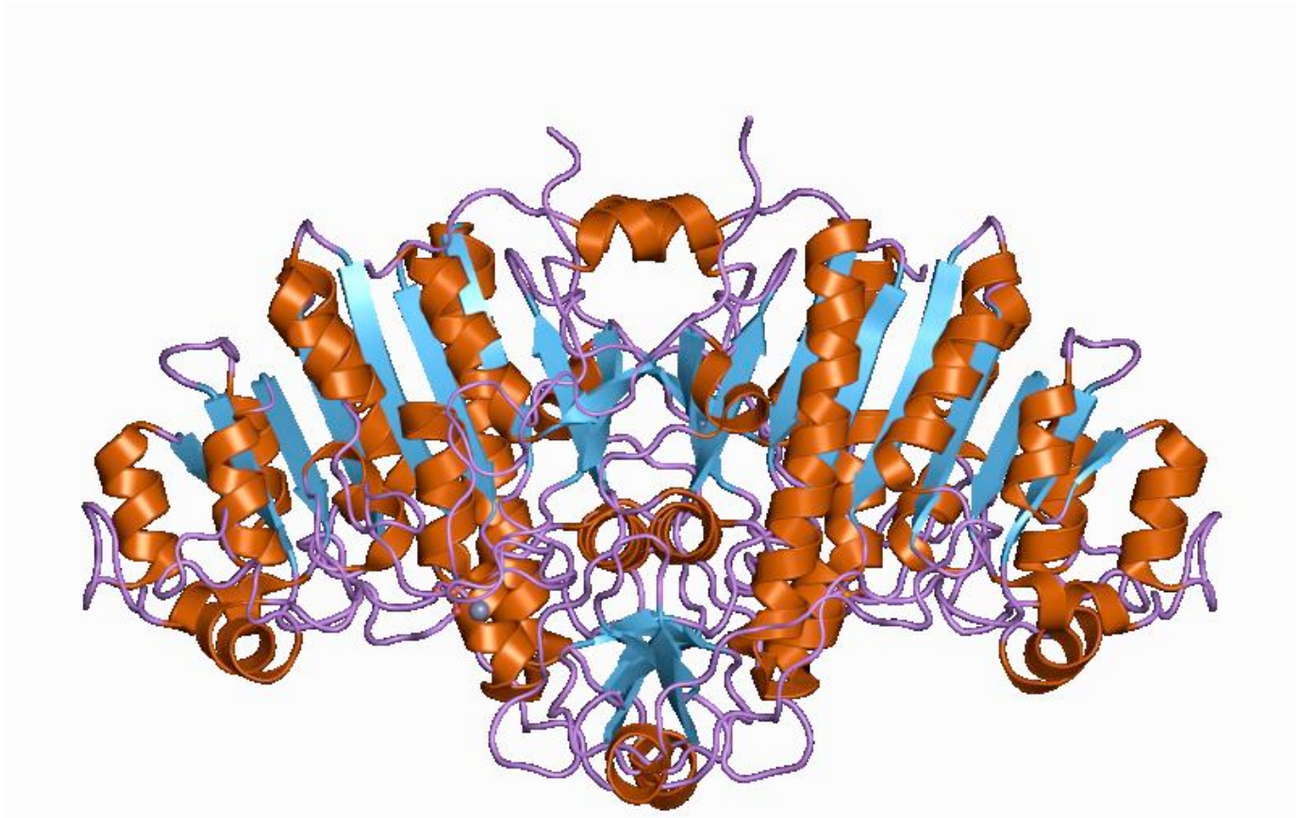


Source: Koenig and Weigel (2015)

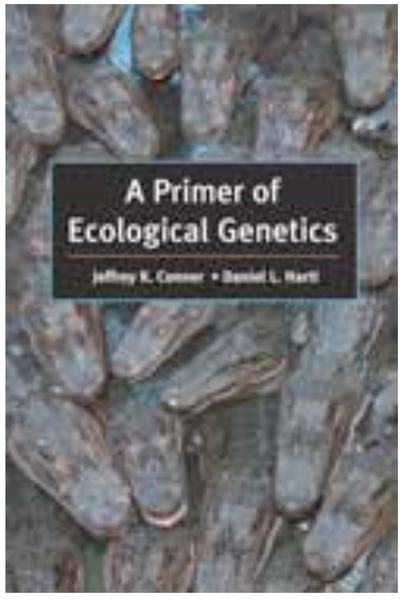
Outcrossing is maintained as long as the fitness loss due to inbreeding depression is greater than the benefit of assured reproduction and the inherent double benefit of selfing alleles in an outcrossing population. Selfing results in an increased rate of genetic drift, which reduces the power of selection and reduces genetic diversity. These combined effects may contribute to increased extinction rates in selfers.




MORE
THINGS
CONSIDERED



Alkaline phosphatase (ALP, ALKP) is a hydrolase enzyme responsible for removing phosphate groups from many types of molecules including nucleotides.



"...genetic drift increases homozygosity and decreases heterozygosity without changing allele frequencies..."

"...exactly the same pattern produced by inbreeding..."

"...Sewall Wright used this similarity between genetic drift and inbreeding to create **F-statistics**, which provide an integrated view of genetic variation at three hierarchical levels of population structure..."

> the "inbreeding" due to small population size is actually a consequence of genetic drift, not mating with relatives more often than expected by chance

> inbreeding increases the frequencies of both homozygotes (AA and aa) and therefore the sub-population deviates from HWE

> genetic drift increases the frequencies of only one - the homozygote as one allele randomly heads to fixation, and the sub-population stays in HWE.

> Departure from HW expected genotype frequencies, the autozygosity or inbreeding coefficient and the fixation index are all interrelated.

The probability that two uniting gametes in an individual came from a male grandparent is:

$$\frac{1}{2}\times\frac{1}{2}=\frac{1}{4}$$

The probability that both gametes come from the same male / female is:

$$\frac{1}{N_m} \qquad \frac{1}{N_f}$$

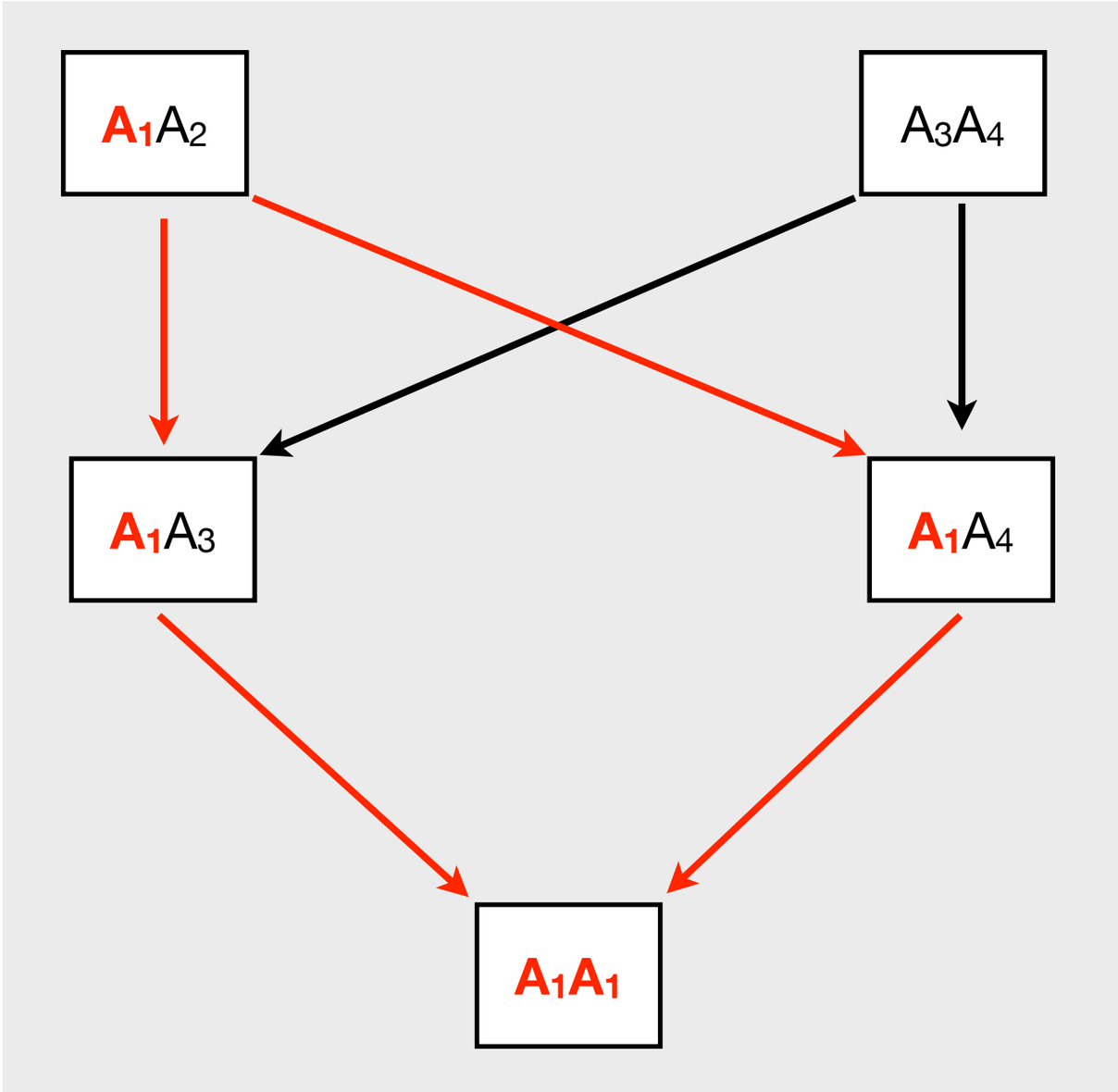
The combined probability that both uniting gametes come from the same grandfather is:

$$\frac{1}{4N_m}$$

The same probabilities hold for grandmothers:

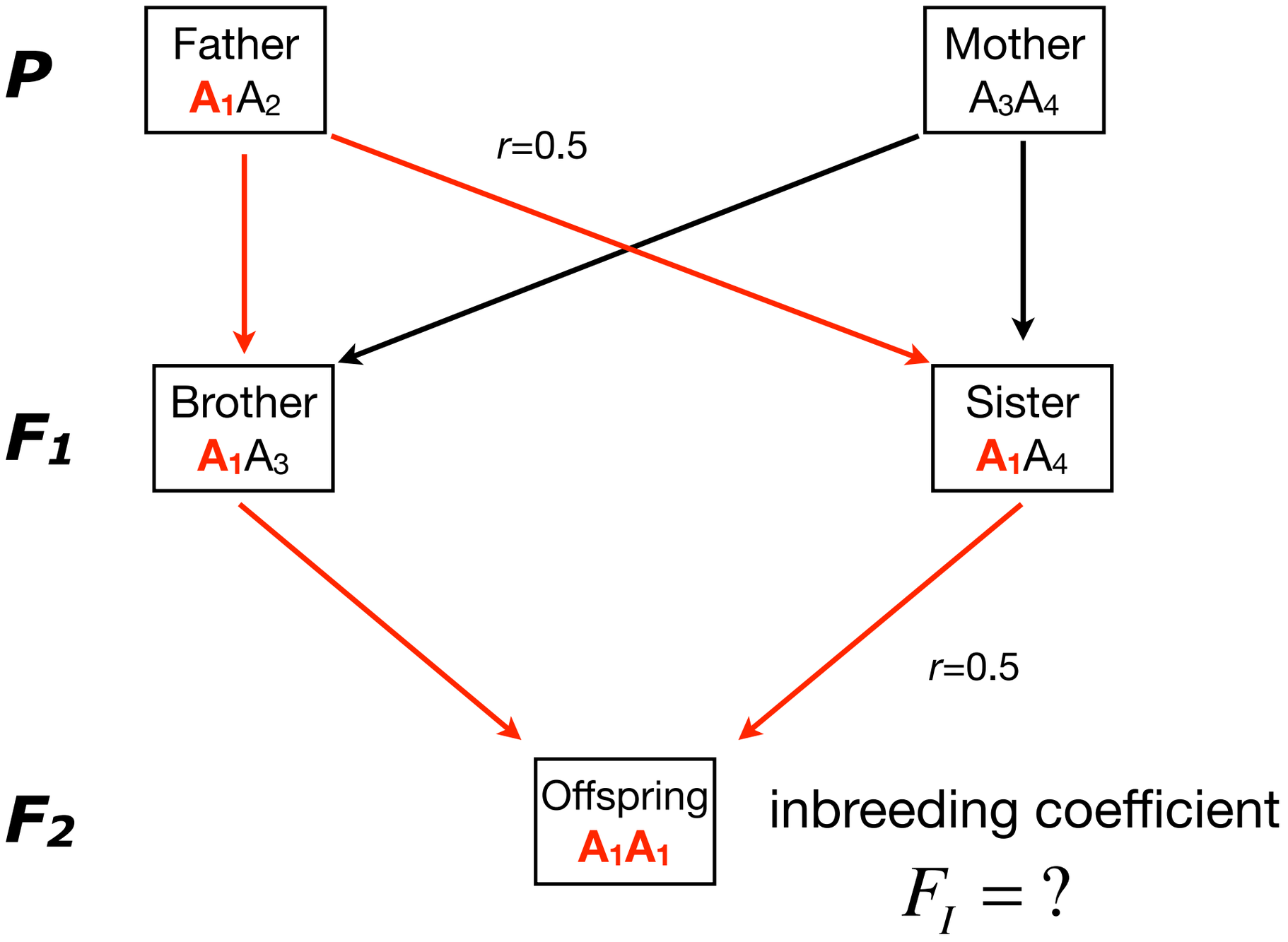
$$\frac{1}{4N_F}$$

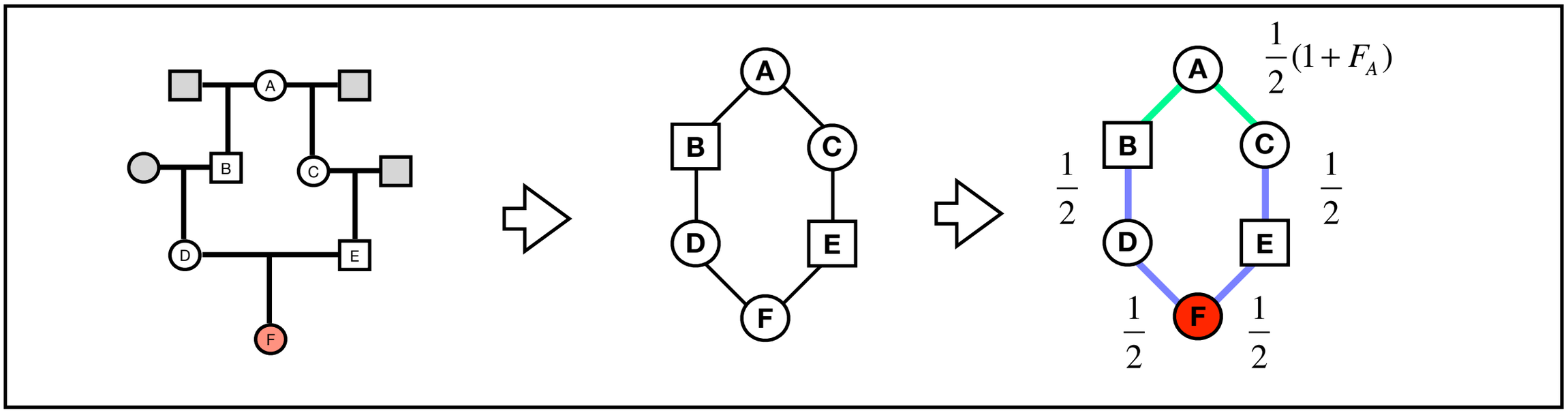
The combined probability of uniting gametes coming from the same grandparent is:



$$\frac{1}{4N_m}+\frac{1}{4N_f}=\frac{1}{N_e}$$

r : coefficient for relatedness



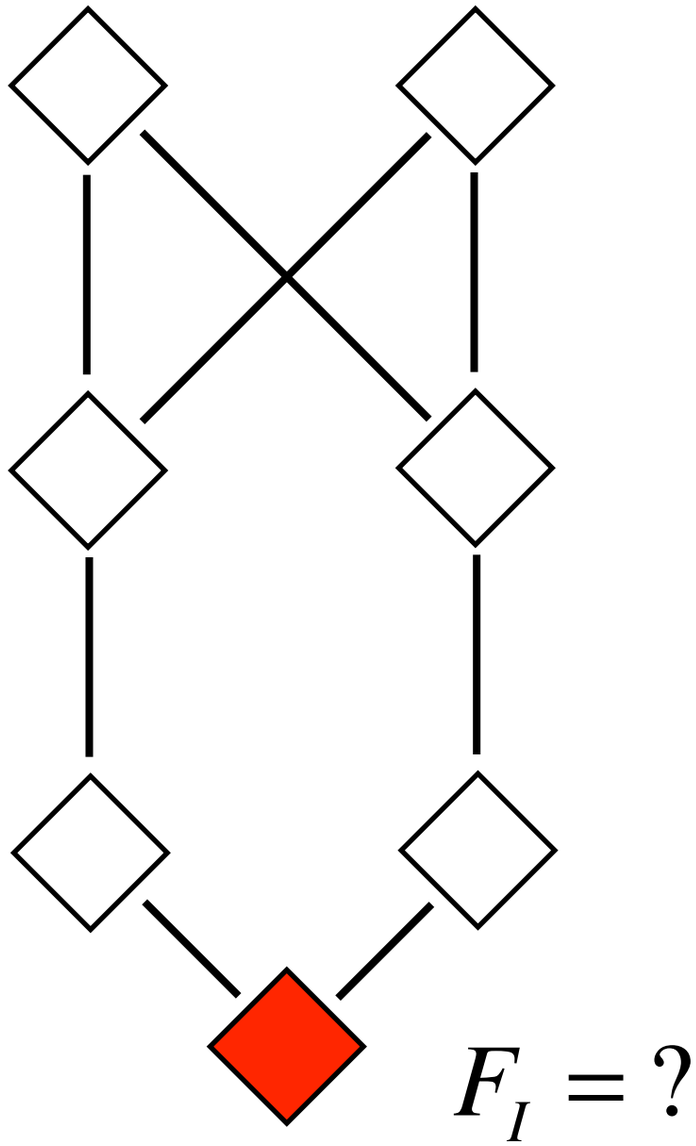


a. identify all common ancestors in the pedigree → F_A

b. trace all the paths of gametes (DB<u>A</u>CE) → i

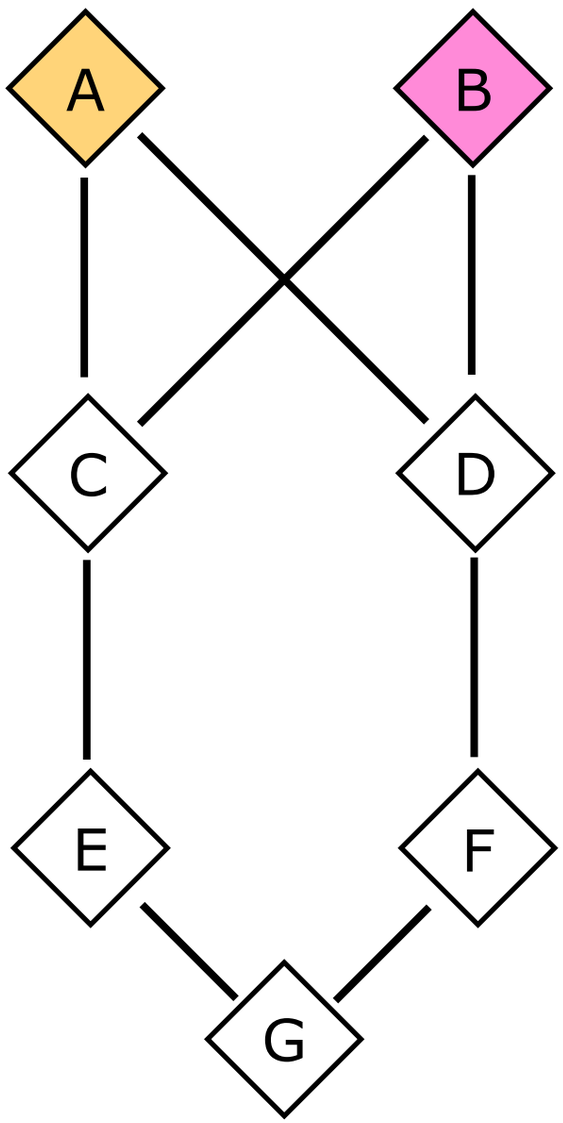
c. calculate inbreeding coefficient → F_I

$$F_I = \left(\frac{1}{2}\right)^i (1+F_A) \overset{F_A=0}{\Rightarrow} \left(\frac{1}{2}\right)^5 = \frac{1}{32}$$


$F_I = ?$

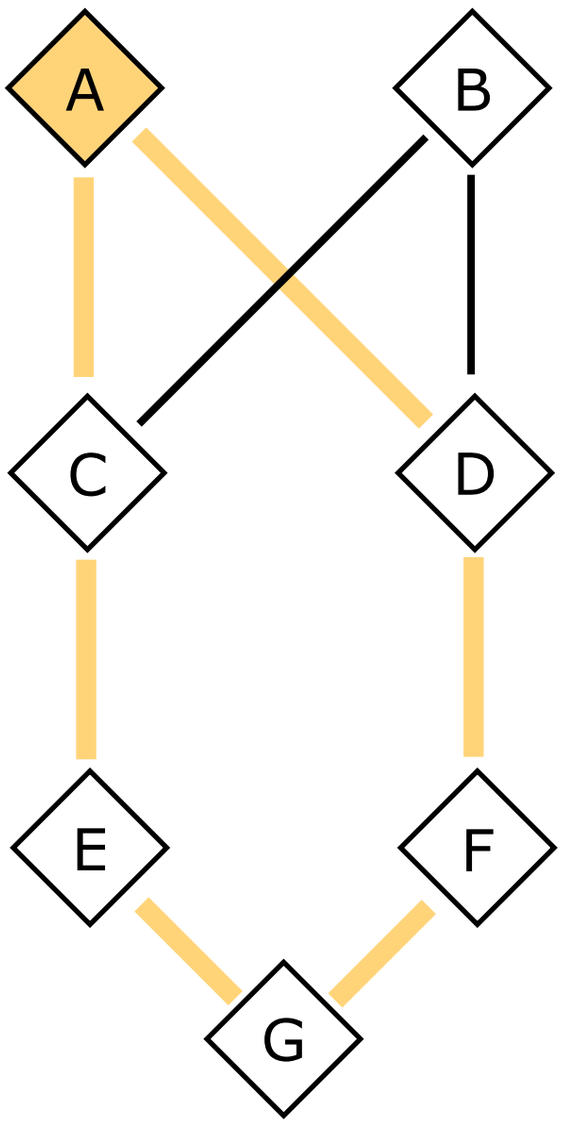
a. identify all common ancestors in the pedigree

$F_A = 0$



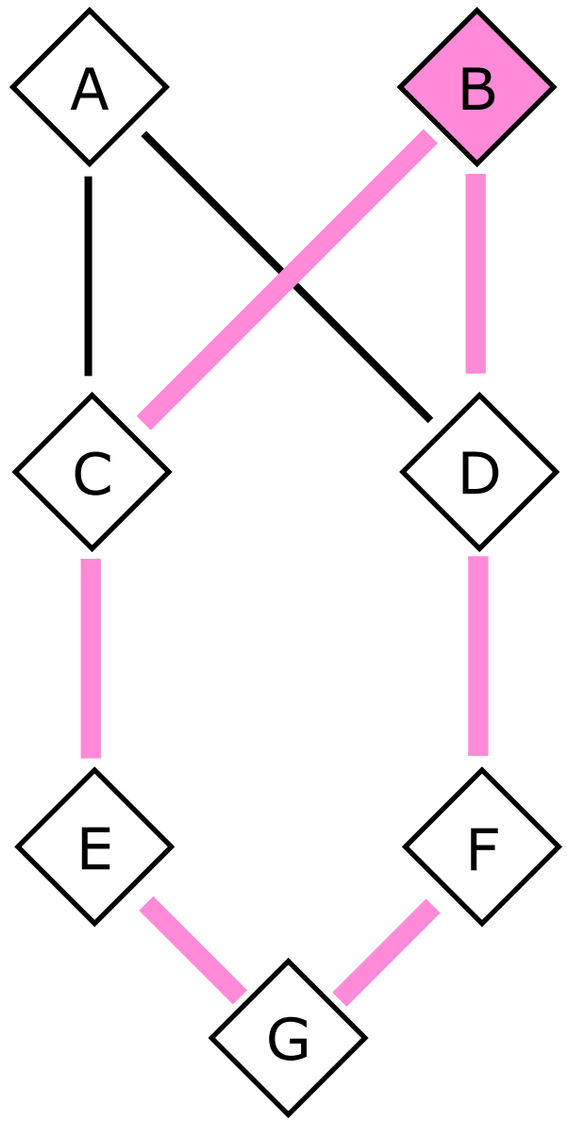
$F_B = 0$

b. trace all the paths of gametes



E-C-**A**-D-F

i=5



E-C-**B**-D-F

i=5

c. calculate inbreeding coefficient F_I

$$F_{G(A)} = \left(\frac{1}{2}\right)^5 (1 + F_A) \overset{F_A = 0}{\Rightarrow} \left(\frac{1}{2}\right)^5 = \frac{1}{32}$$

$$F_{G(B)} = \left(\frac{1}{2}\right)^5 (1 + F_B) \overset{F_B = 0}{\Rightarrow} \left(\frac{1}{2}\right)^5 = \frac{1}{32}$$

$$F_G = F_{G(A)} + F_{G(B)} = \frac{1}{32} + \frac{1}{32} = \frac{1}{16} = 6.25\%$$

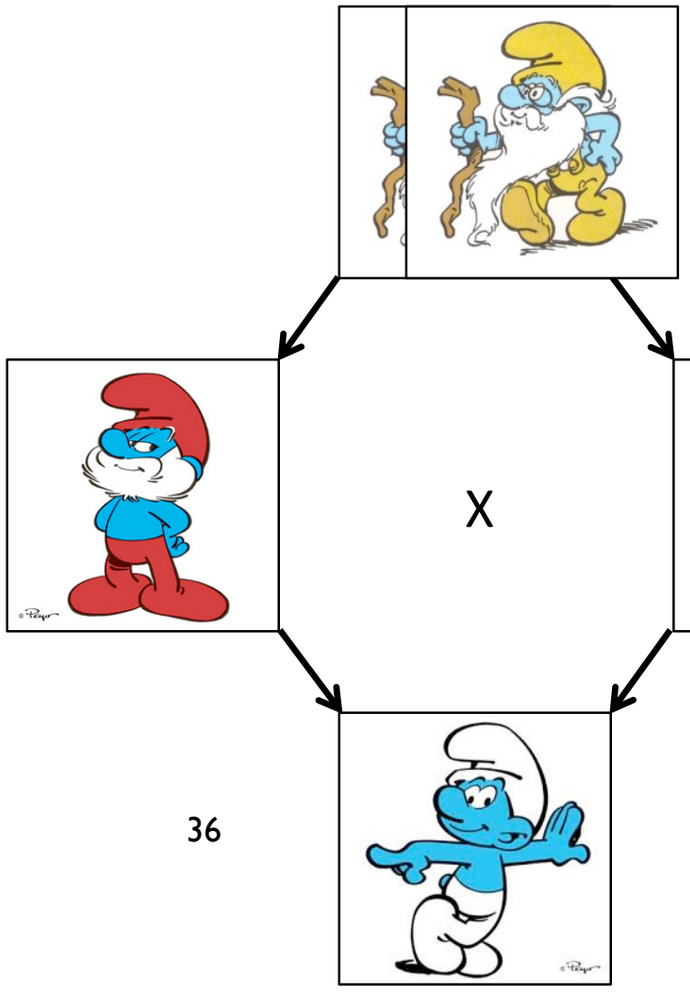
Inbreeding

$$F = \sum \left(\frac{1}{2}\right)^{i} (F_A + 1)$$

Adrian F. Meyer
Stefan Boos
20.12.2011

Definition

Inbreeding is the mating of individuals related by ancestry



Grand-parents

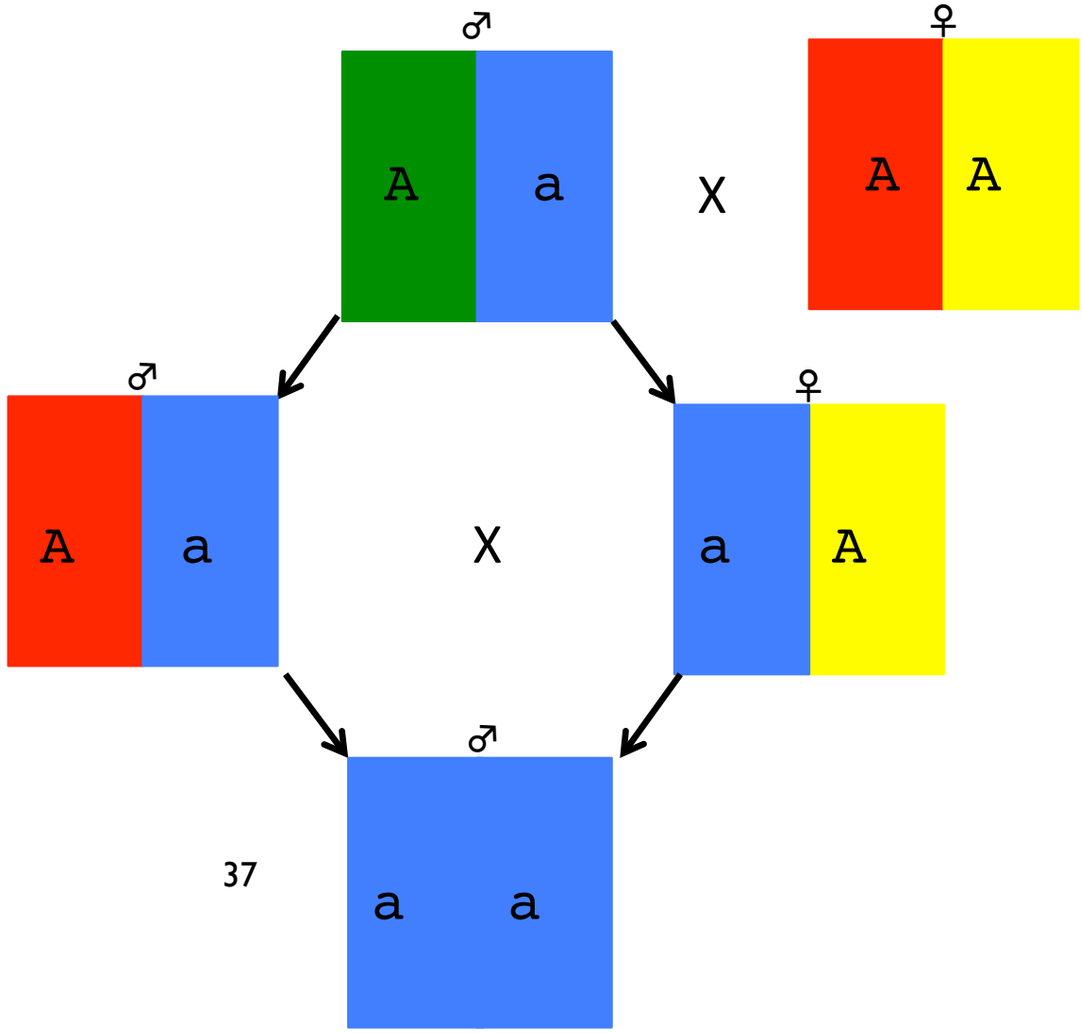
Parents

Inbred offspring

The consequence

An increased probability of inheriting alleles that are copies of the same allele

Locus “A”
Alleles A & a



This leads to increased frequencies of homozygotes

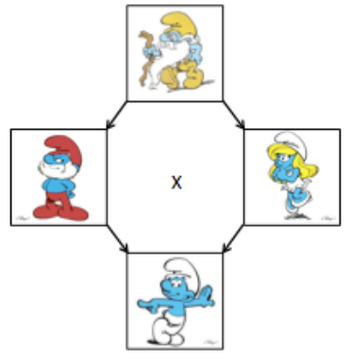
Calculating Inbreeding Coefficient F

$$F = \sum_{i} \left(\frac{1}{2}\right)^{i} (F_A + 1)$$

F_A = Inbreeding Coefficient of the common ancestor

i = Path length

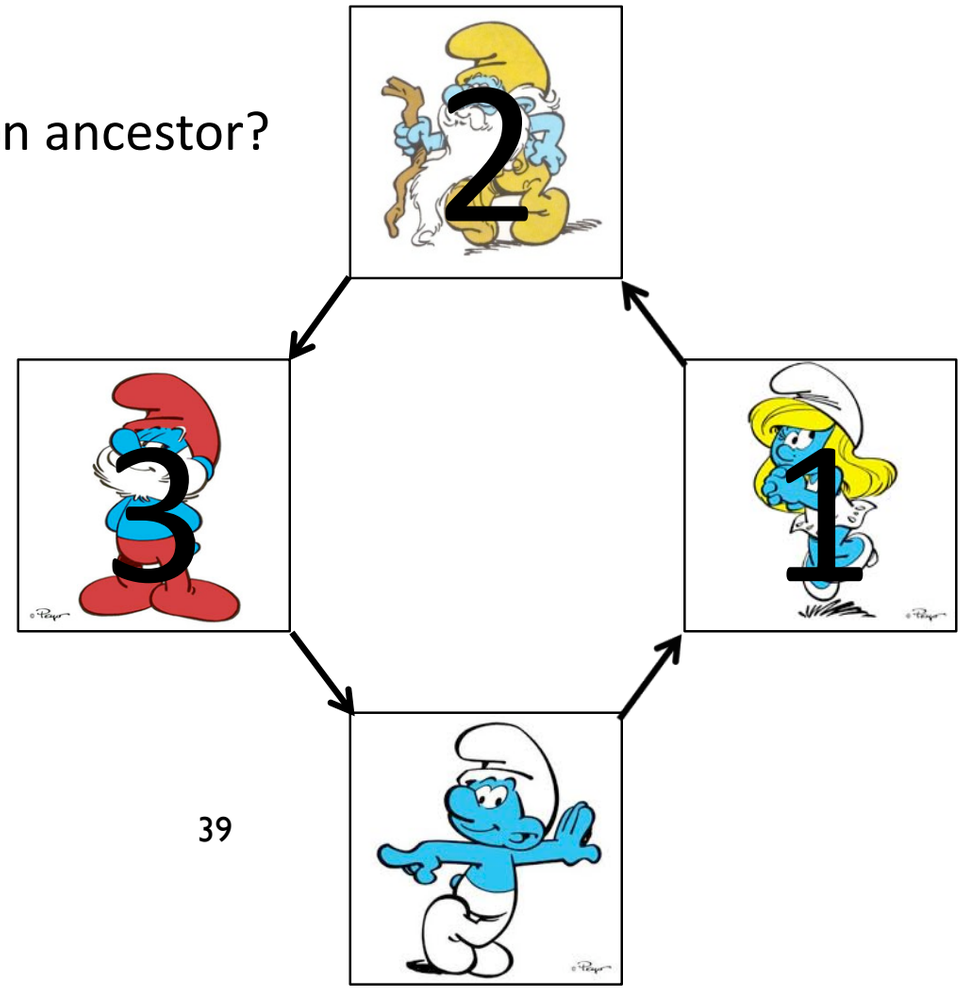
Calculating Inbreeding Coefficient F_Z



2. Who is the common ancestor?

3. How many paths?

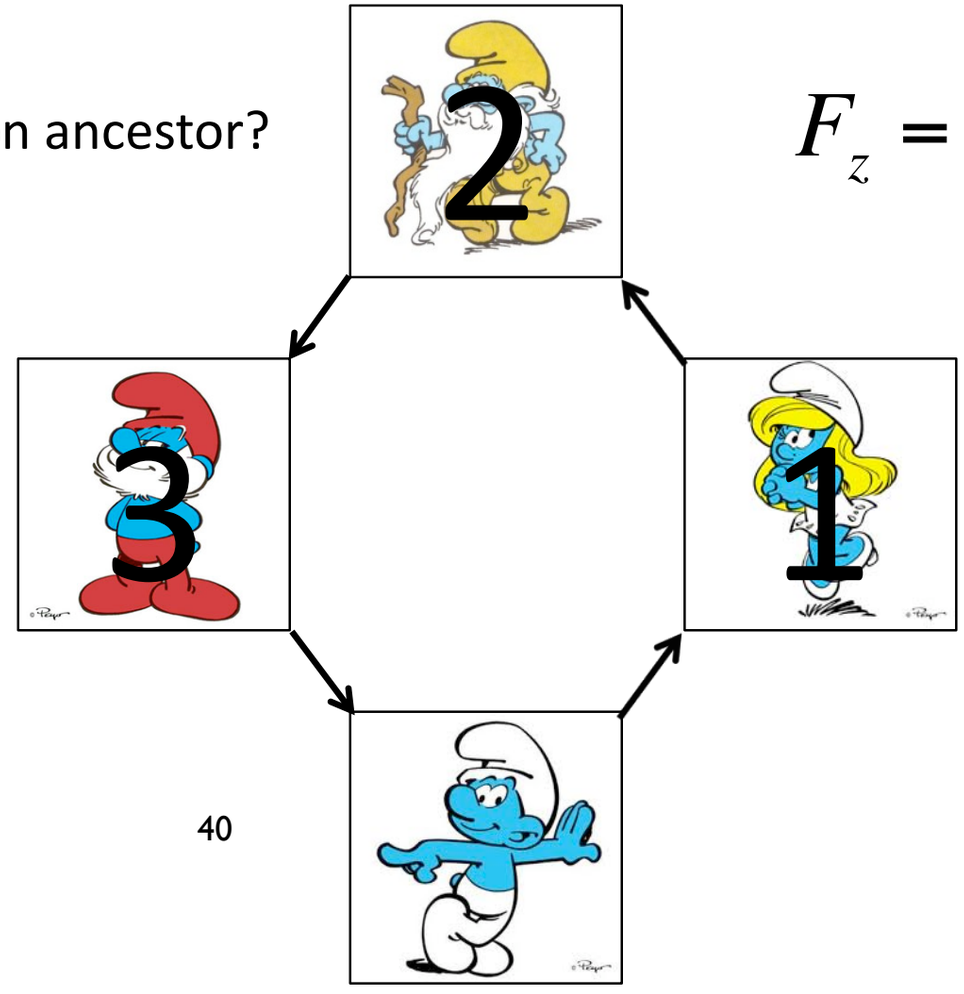
1. Who becomes F?



Calculating Inbreeding Coefficient F_Z

2. Who is the common ancestor?

F_A = 0



3. How many paths?

i = 3

$$F_z = \sum \left(\frac{1}{2}\right)^i (F_A + 1)$$

1. Who becomes F?

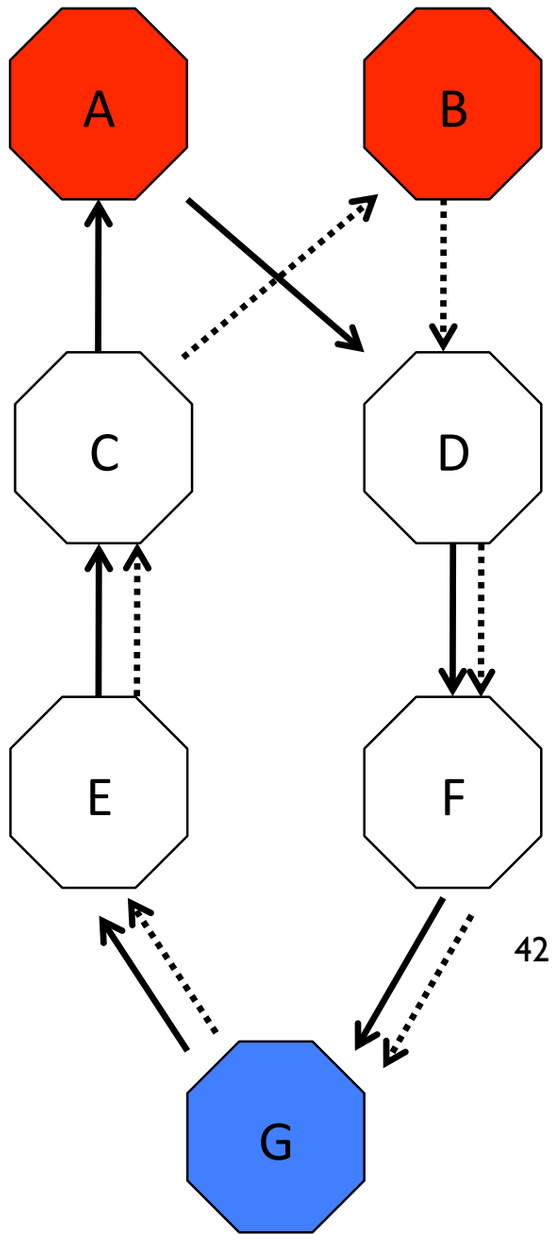
F_Z = 0.125 = 12.5%

2 further Examples

Two common Ancestors

A real example

Two common Ancestors



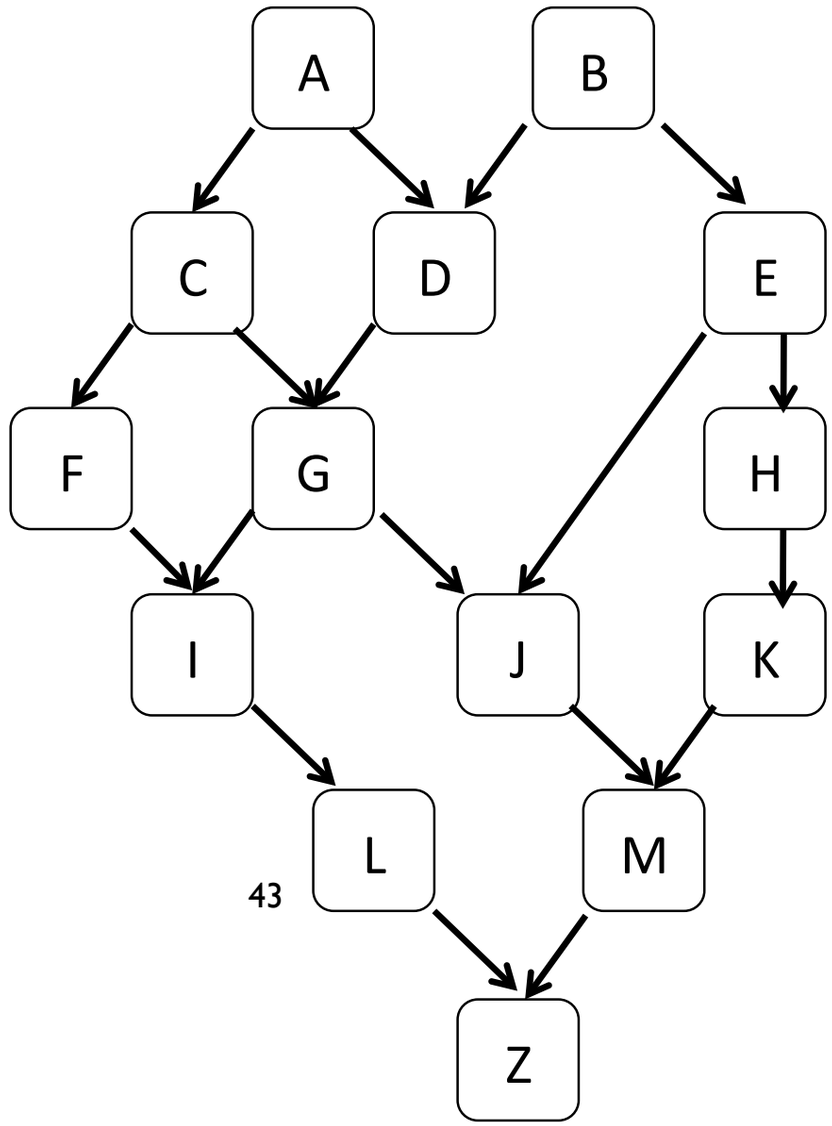
	paths	$1 + F_{A/B}$
A	i = 5	1 + 0
B	i = 5	1 + 0

$F_{G(A)} = (1/2)^5 * (1+0) = 1/32$

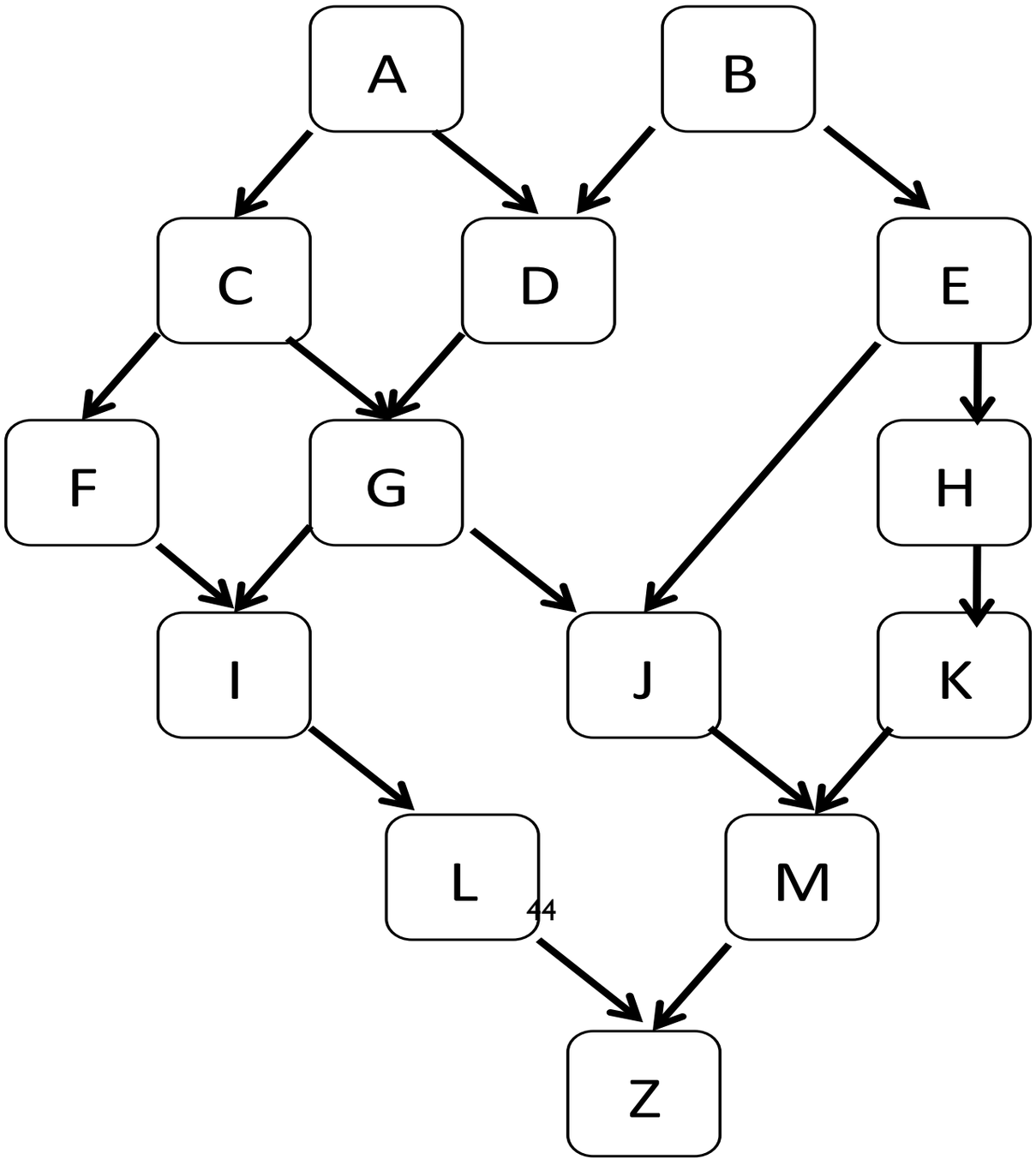
$F_{G(B)} = (1/2)^5 * (1+0) = 1/32$

$F_G = 1/16 =$ **6.25%**

A real Example

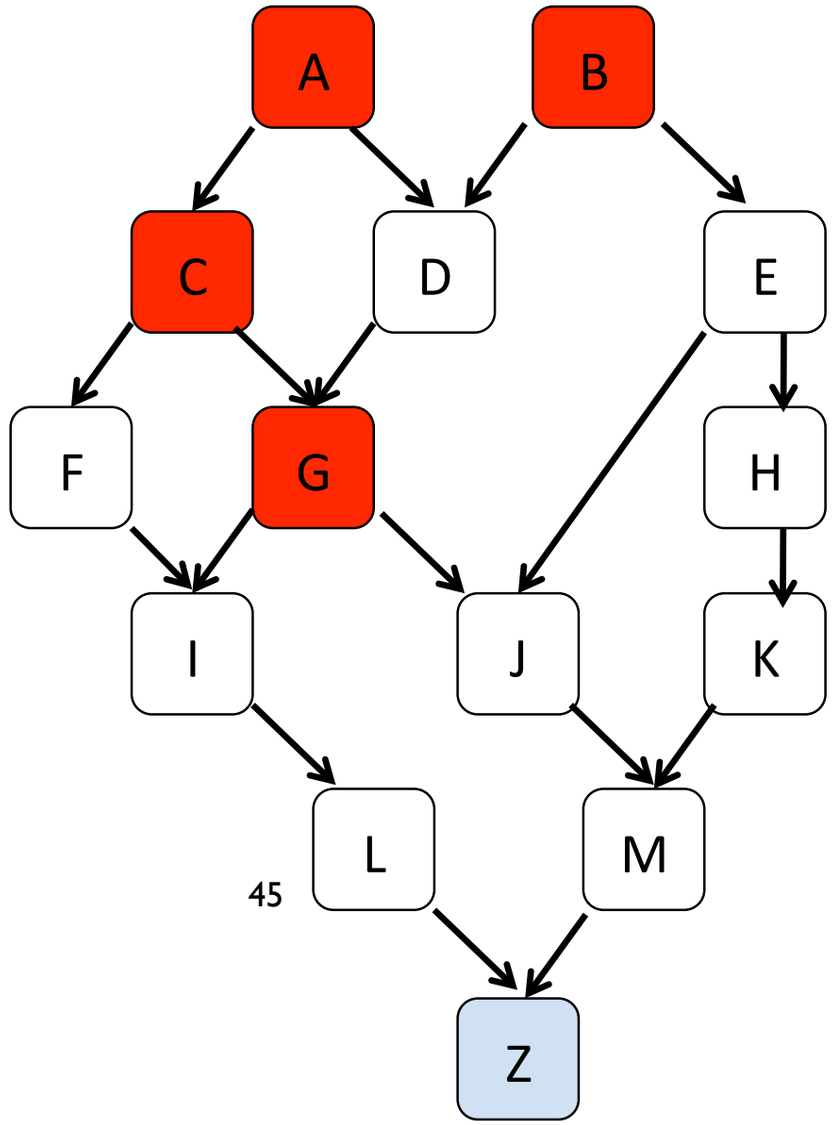


Ragusa Challenge



$F_Z = ?\%$

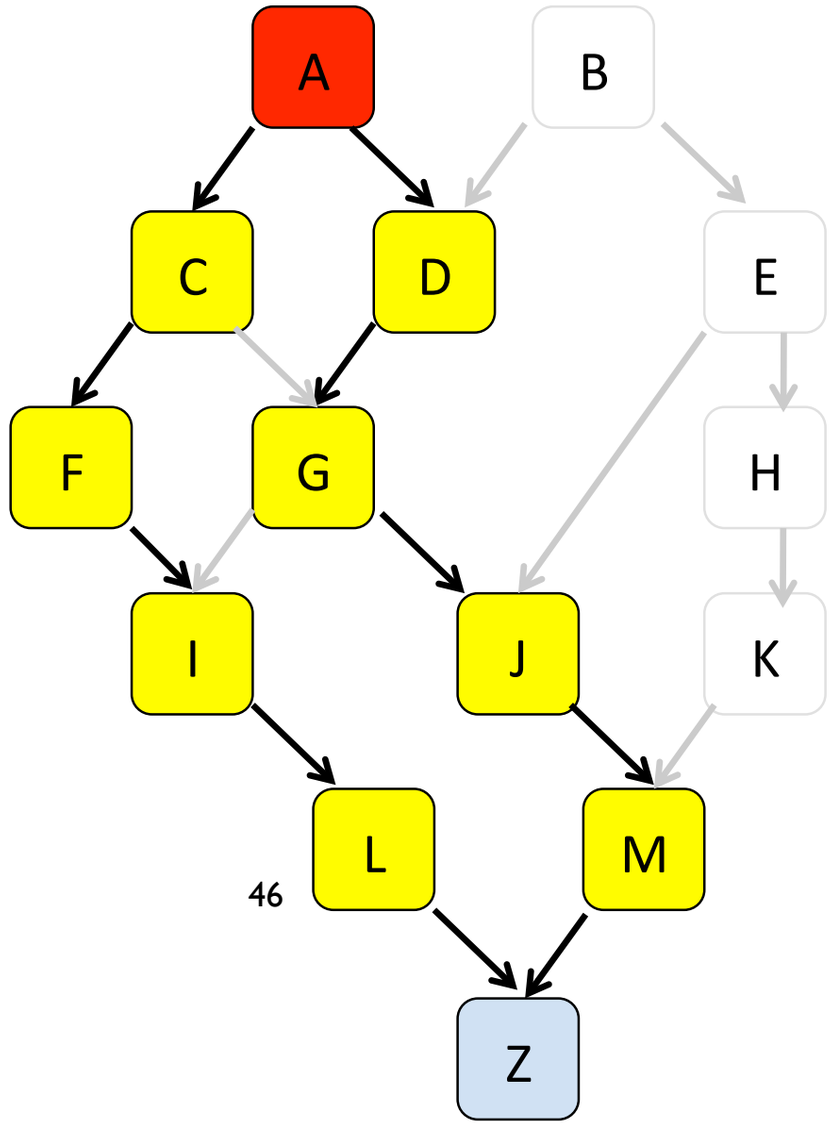
Common Ancestors



Path: M J G D A C F I L

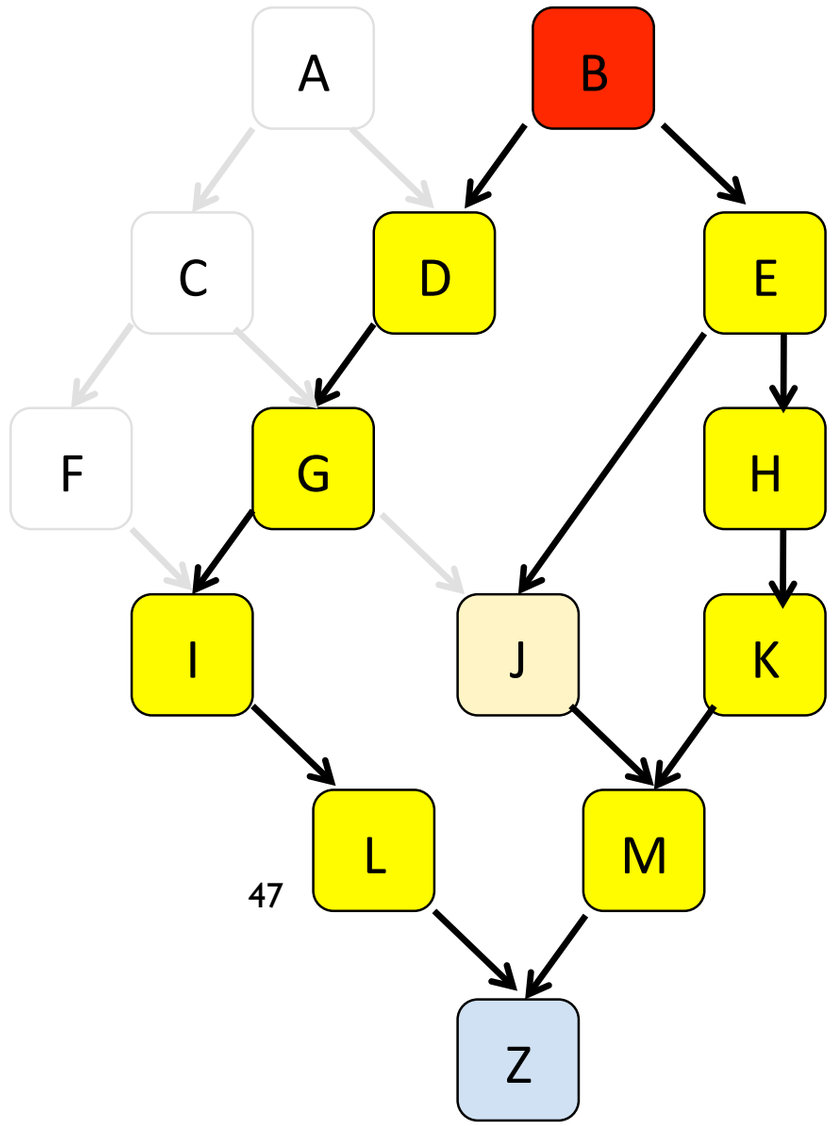
$F_{Z(A)} = (1/2)^{i} * (F_A + 1) = (1/2)^{9} * (0 + 1) = 0.002 = \mathbf{0.2\%}$

$F_{Z(A)}$



M K H E <u>B</u> D G I L $F_{Z(B1)} = (1/2)^{i} * (F_B+1) = (1/2)^{9} * (0 + 1) = 0.002 =$ **0.2%**

M J E <u>B</u> D G I L $F_{Z(B2)} = (1/2)^{i} * (F_B+1) = (1/2)^{8} * (0 + 1) = 0.004 =$ **0.4%**

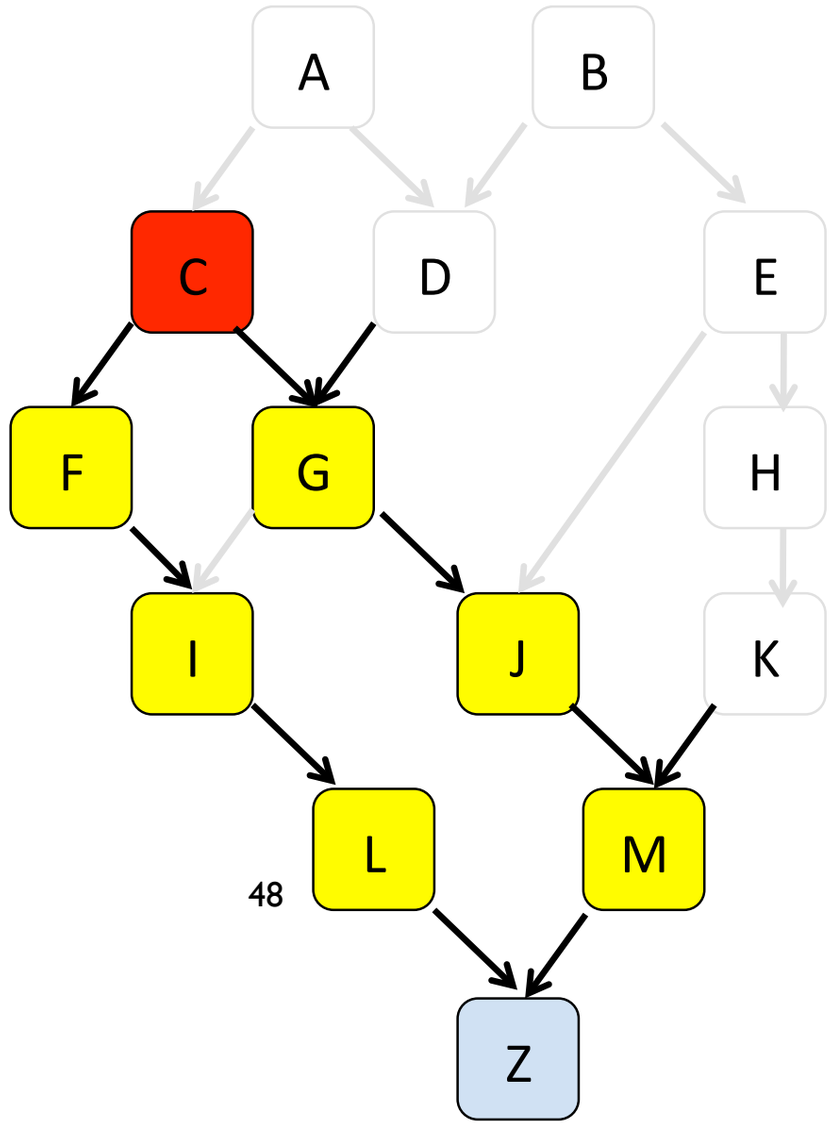


$F_{Z(B)}$

M J G C F I L

$F_{Z(C)} = (1/2)^{i*} (F_C+1) = (1/2)^{7*} (0 + 1) = 0.008 =$ **0.8%**

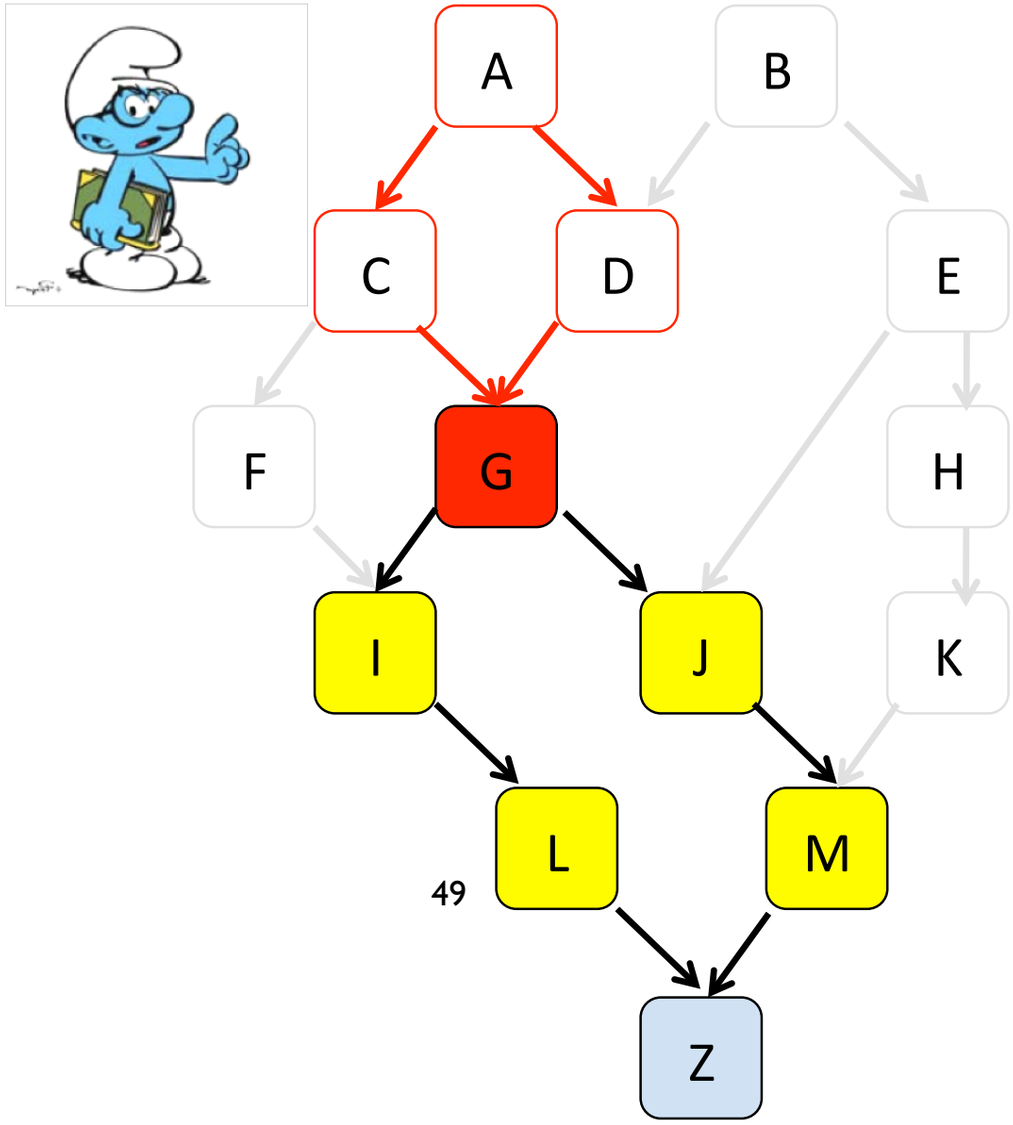
$F_{Z(C)}$



L I G J M

$F_{Z(G)} = (1/2)^{i} * (F_G+1) = (1/2)^{5} * (\mathbf{0.125} + 1) = 0.035 = \mathbf{3.5\%}$

$F_{Z(G)}$



Total F_z

$F_{Z(A)}$	0.2%
$F_{Z(B1)}$	+ 0.2%
$F_{Z(B2)}$	+ 0.4%
$F_{Z(C)}$	+ 0.8%
$F_{Z(G)}$	+ 3.5%
F_Z	**= 5.1%**

Rounded values

Question

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