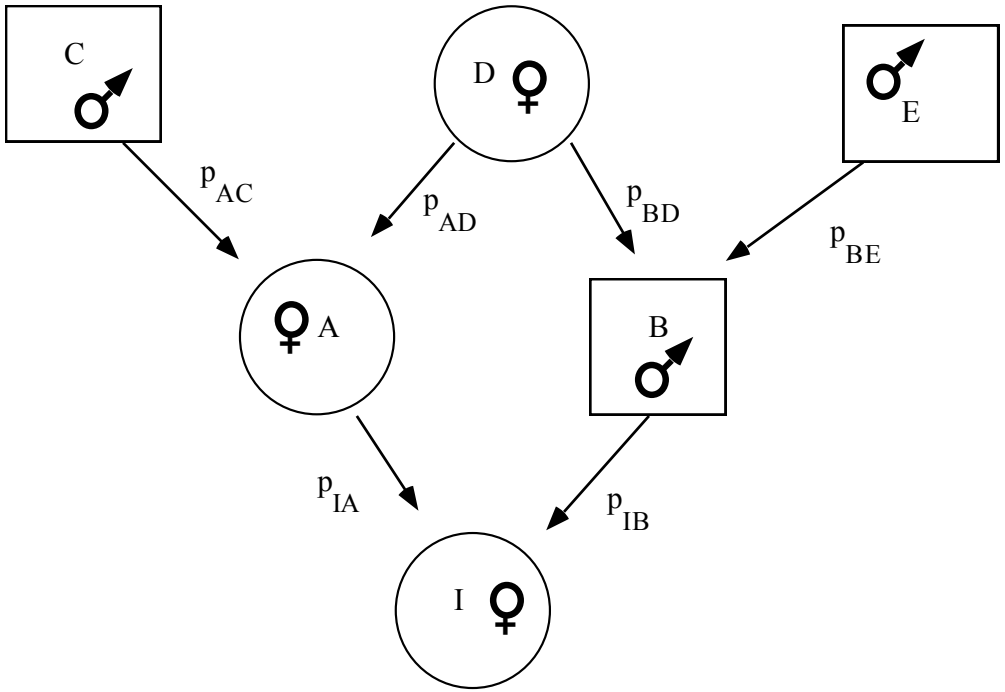
Pedigree Inbreeding

Or

Just How Inbred am I?

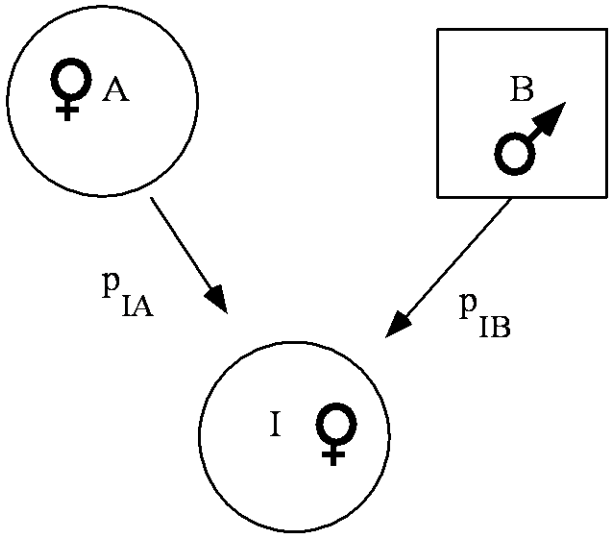
(This stuff is not in the book)

What is a Pedigree?



A pedigree is a set of relationships due to mating structure

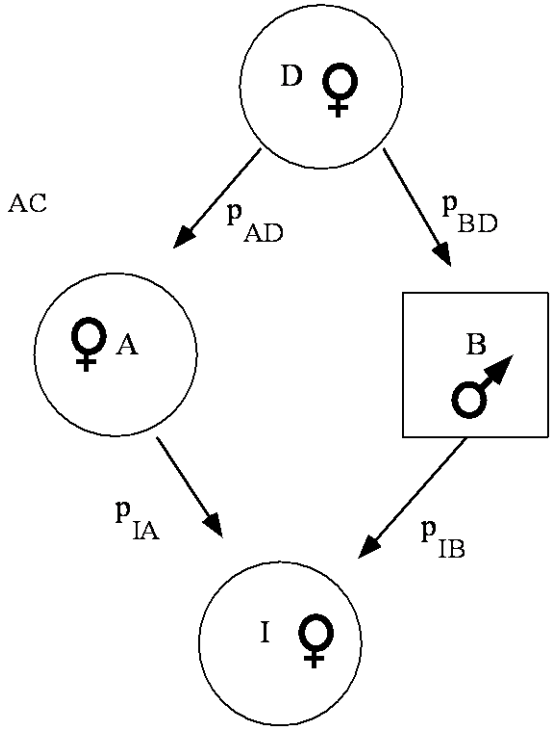
How inbred is an individual?



In this case not at all. There is no path of relatedness from I Back to I.

How inbred is an individual?

In This case the relatedness is 1/8.



The general formula is $f = \left(\frac{1}{2}\right)^N$

Where f = the inbreeding coefficient
N = the number of “nodes” in the path (here N=3)

An Example

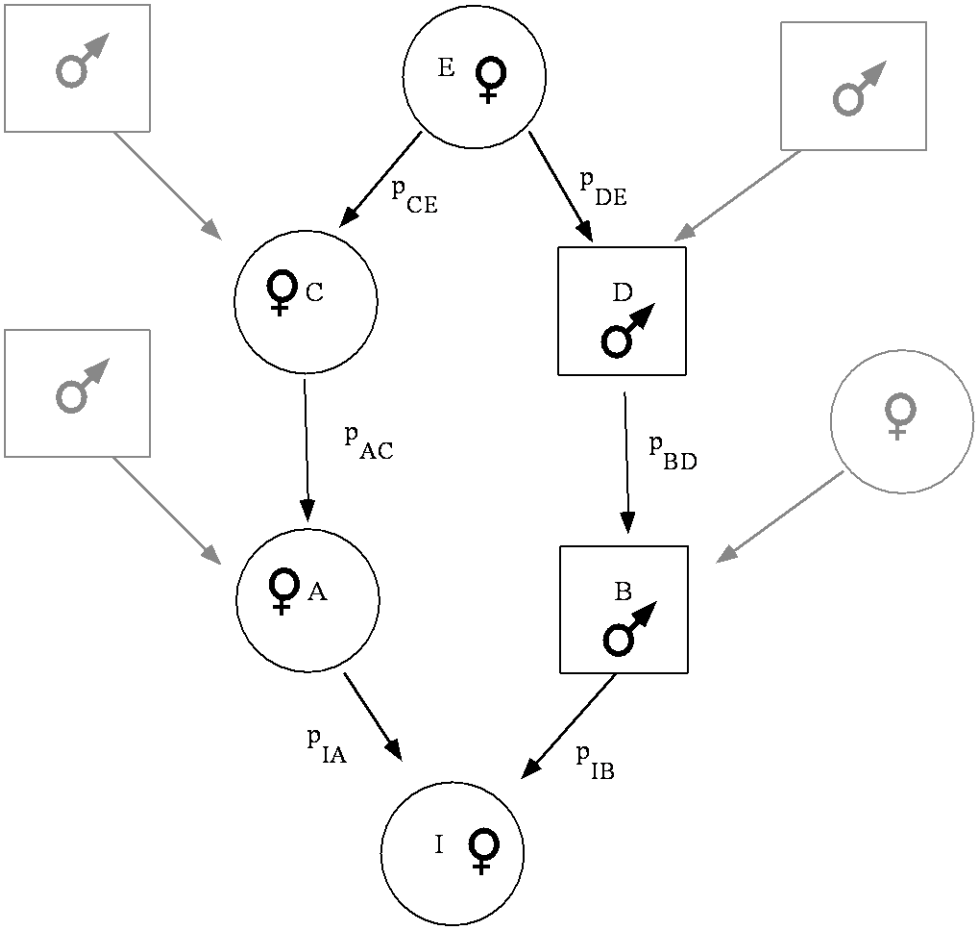
Number of Nodes = 5

Inbreeding Coefficient:

$$f = \left(\frac{1}{2}\right)^N = \left(\frac{1}{2}\right)^5$$

$$= 0.03125$$

$$= \frac{1}{32}$$



The progeny of first 1/2 cousins have an inbreeding coefficient of 1/32. What if they were full first cousins?

Full First Cousins

There are now two paths:

IACEDBI

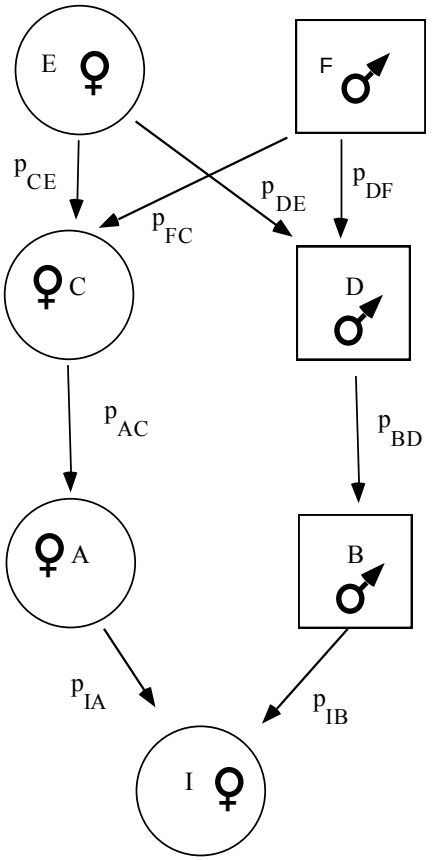
IACFDBI

Nodes/path = 5

$$f = \left(\frac{1}{2}\right)^{N_1} + \left(\frac{1}{2}\right)^{N_2} = \left(\frac{1}{2}\right)^{5} + \left(\frac{1}{2}\right)^{5}$$

$$= 0.03125 + 0.03125$$

$$= \frac{1}{16}$$



The progeny of first cousins have an inbreeding coefficient of 1/16.

Da Rules

1. find all of the paths
2. for each path count the number of nodes
3. the contribution to the inbreeding coefficient for each path is $\left(\frac{1}{2}\right)^N$
4. The inbreeding coefficient is the sum of the contributions of the individual paths.

Why do we care?

1. this pedigree inbreeding is entirely different than the "drift" inbreeding we have talked about.
2. It gives me a chance to talk about F_{IS} and F_{ST}, terms you will hear thrown about, but rarely defined.
3. Every once in a while it does some funny genetic things to a population.

So, Now the Musical Question

What is the inbreeding coefficient of a an individual that is:

1. in an inbred population and
2. the product of brother sister mating?

Recognize that both of these processes make alleles Identical By Descent. But note, that once alleles are IBD, further inbreeding doesn't change anything. Thus, if the alleles in an individual are IBD due to population inbreeding, the fact that they are the result if brother sister mating is of no consequence!

F_{IT}, F_{IS}, F_{ST}

Sewall Wright (one of our persistent heros) came up with the solu

F_{IT} = the inbreeding of an Individual relative to the Total metapopulation = the probability of being IBD

F_{IS} = the inbreeding of an Individual relative to the Subpopulation = the “pedigree” inbreeding

F_{ST} = the inbreeding of the Subpopulation relative to the Total metapopulation = the “drift” inbreeding

F_{IT}, F_{IS}, F_{ST}

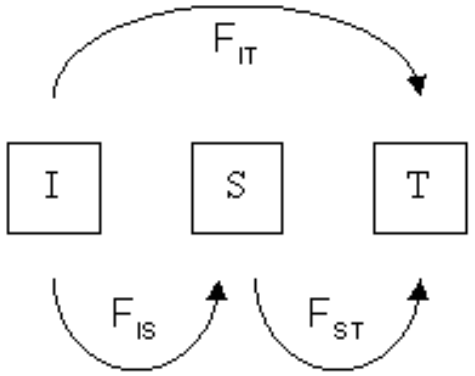
Now here's the trick

It is hard to work with homozygosity (F), but easy to work with heterozygosity (1-F)

It turns out $(1-F_{IT}) = (1-F_{IS})(1-F_{ST})$

Or more usefully:

$$F_{IT} = F_{IS} + F_{ST}(1-F_{IS})$$
$$F_{IT} = F_{ST} + F_{IS}(1-F_{ST})$$



Prairie Dogs!

Prairie dogs: Females stay in the home coterie
Males move to a different coterie

coterie: local group of prairie dogs.

Prairie Dogs!

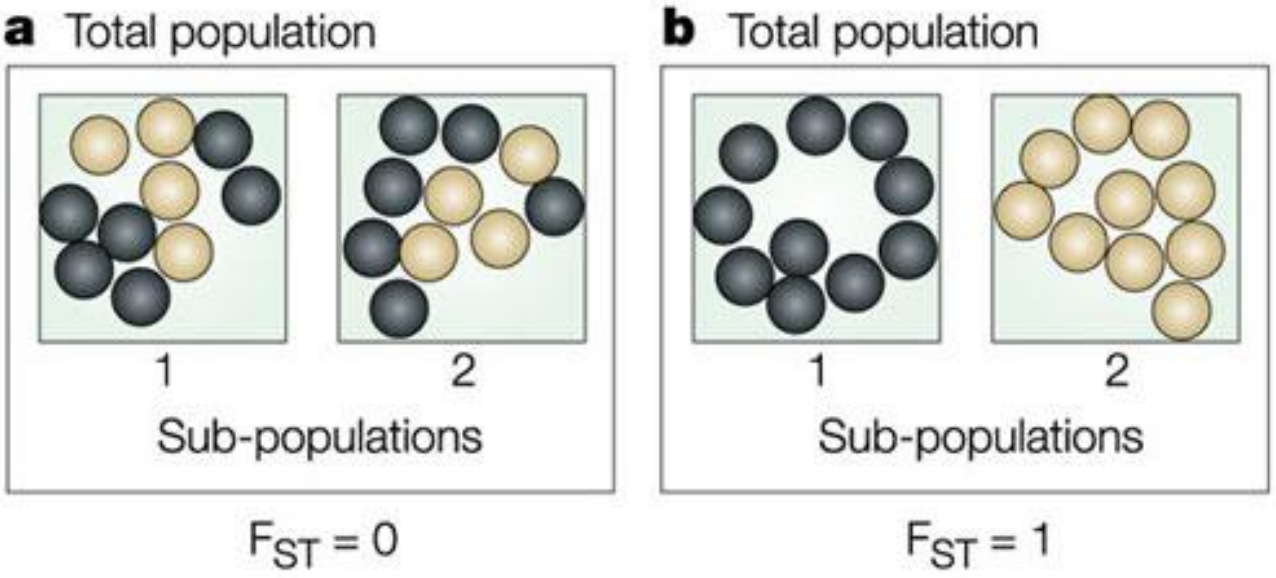
Females stay in the home coterie

Females are sisters and share many genes
FST tends to be high.

Males move to a different coteri

Fathers come from different coteries.
Children are very outbred (much more than expected)
F_{IS} is NEGATIVE!!!!!!!!!

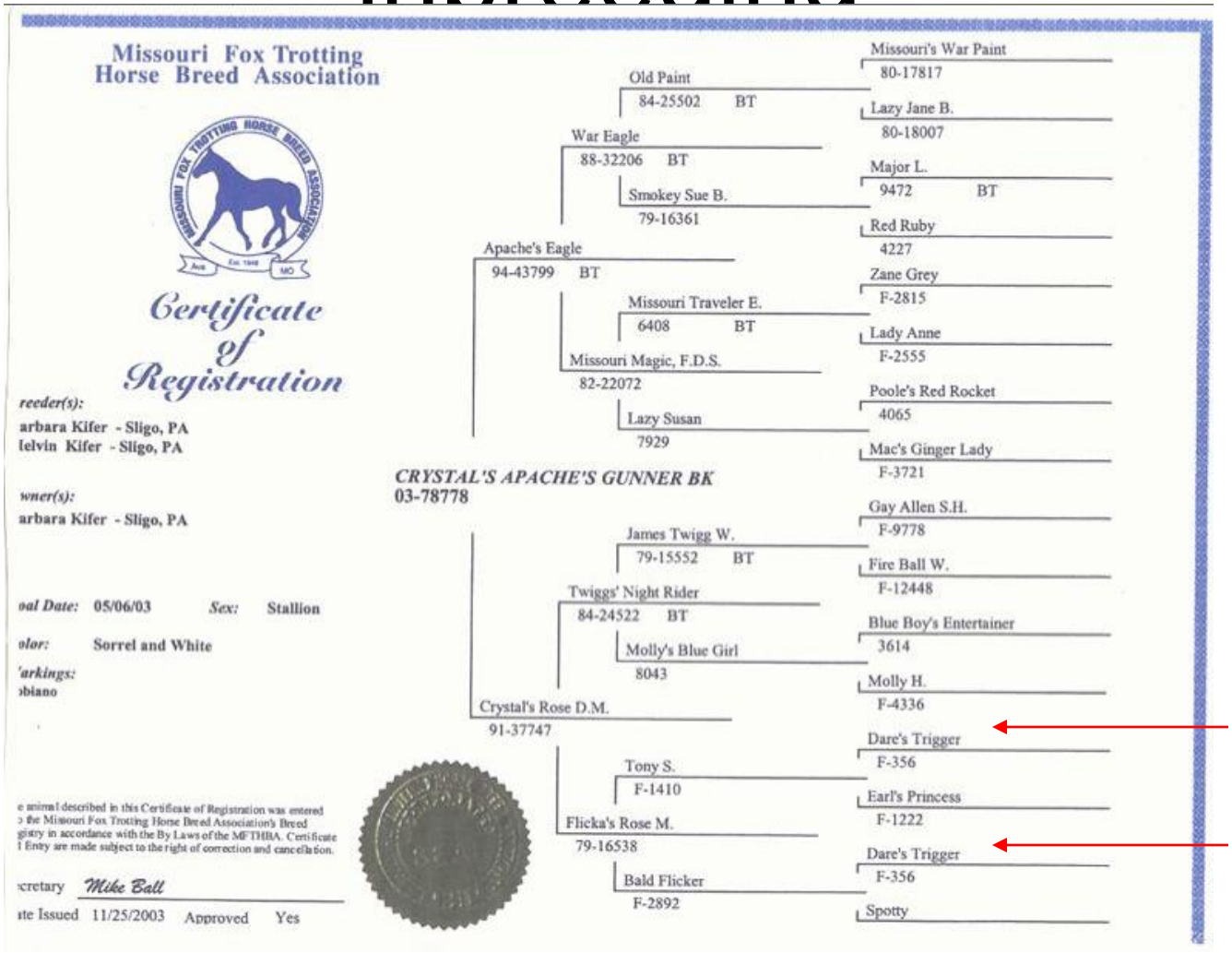
FST measures Population Structure



FST measures Population Structure

Genetic tree drawn from ABI Linkage Mapping SetsFrom the allele frequencies of 45 markers in ABI Linkage Mapping Sets (panels 13 through 16), we computed FST genetic distances (Wright, 1951). FST is a simple measure of genetic differentiation and is estimated as a standardized variance of allele frequencies between two populations. Next, we represented the genetic distance matrix as a neighbor-joining tree (Saitou and Nei, 1987). We also estimated a level of confidence for every branch with a bootstrap approach (Felsenstein, 1985). The figures shown above the tree branches represent the number of times (expressed as a percentage) in which that branch was found among 1,000 bootstrapped trees.

F_{IS} measures pedigree inbreeding



Missouri Fox Trotting Horse Breed Association

Certificate of Registration

reeder(s):
arbara Kifer - Sligo, PA
lelvin Kifer - Sligo, PA

wner(s):
arbara Kifer - Sligo, PA

oal Date: 05/06/03 Sex: Stallion

olor: Sorrel and White

'arkings:
obiano

e animal described in this Certificate of Registration was entered
o the Missouri Fox Trotting Horse Breed Association's Breed
gistry in accordance with the By Laws of the MFTHBA. Certificate
l Entry are made subject to the right of correction and cancellation.

ecretary Mike Ball

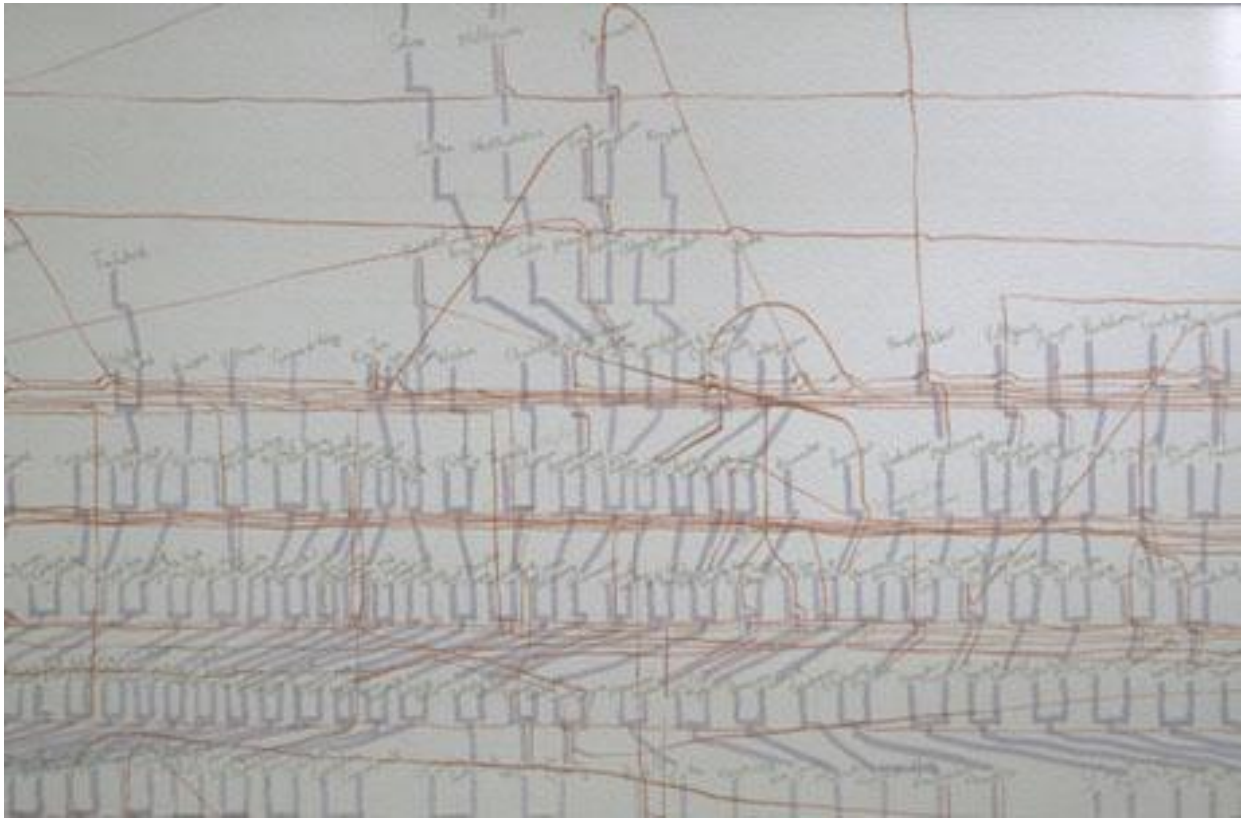
te Issued 11/25/2003 Approved Yes

CRYSTAL'S APACHE'S GUNNER BK
03-78778

Old Paint 84-25502 BT
War Eagle 88-32206 BT
Smokey Sue B. 79-16361
Apache's Eagle 94-43799 BT
Missouri Traveler E. 6408 BT
Missouri Magic, F.D.S. 82-22072
Lazy Susan 7929
James Twigg W. 79-15552 BT
Twiggs' Night Rider 84-24522 BT
Molly's Blue Girl 8043
Crystal's Rose D.M. 91-37747
Tony S. F-1410
Flicka's Rose M. 79-16538
Bald Flicker F-2892

Missouri's War Paint 80-17817
Lazy Jane B. 80-18007
Major L. 9472 BT
Red Ruby 4227
Zane Grey F-2815
Lady Anne F-2555
Poole's Red Rocket 4065
Mac's Ginger Lady F-3721
Gay Allen S.H. F-9778
Fire Ball W. F-12448
Blue Boy's Entertainer 3614
Molly H. F-4336
Dare's Trigger F-356
Earl's Princess F-1222
Dare's Trigger F-356
Spotty

One Horse-Meadow Star, 1992



This drawing enumerates all the ancestors of the 1991 Eclipse Award champion, Meadow Star. Inbreeding in the pedigree is marked by red lines. Wherever a name reappears duplicated, a red line loops back to the first occurrence of the name. The more inbred the horse, the more red the whole image becomes.

http://www.genomicart.org/rule.htm

An Example with Numbers

A population has had a population bottleneck of 4 for one generation, and there after has a very large (infinite) population size.

What is the total inbreeding coefficient (F_{IT}) for an individual that is the product of brother sister mating in this population?

F_{ST} = drift inbreeding

F_{IS} = pedigree inbreeding

F_{IT} = Total inbreeding

An Example with Numbers

A population has an effective population size of 4 for one generation, and there after has a very large (infinite) population size.

F_{ST} = drift inbreeding = 1/8

$$F_{ST(t=0)} = 0$$

$$F_{ST(t=1)} = \frac{1}{(2)(4)} + \left(1 - \frac{1}{(2)(4)}\right)(0) = 0.125 = \frac{1}{8}$$

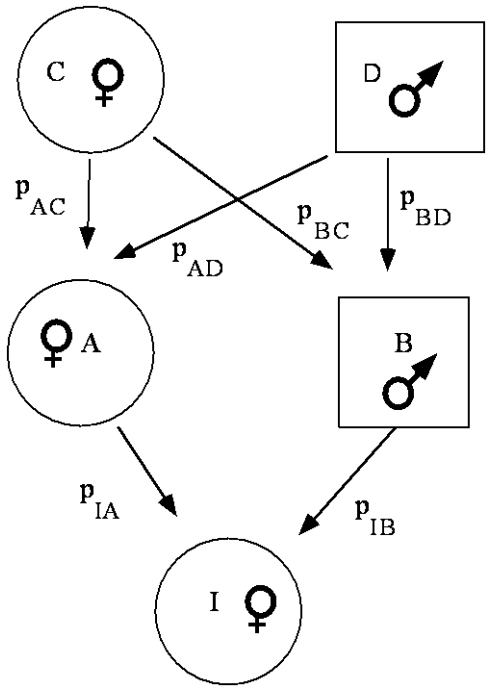
$$F_{ST(t>1)} = \frac{1}{(2)(\infty)} + \left(1 - \frac{1}{(2)(\infty)}\right)\left(\frac{1}{8}\right) = 0.125 = \frac{1}{8}$$

$$F_{ST(t+1)} = \frac{1}{2N} + \left(1 - \frac{1}{2N}\right)F_{ST(t)}$$

An Example with Numbers

. . . the product of brother sister mating

F_{IS} = pedigree inbreeding = 1/4



Path 1 = ACB = 3 nodes
Path 2 = ADB = 3 nodes

$$F_{IS} = \left(\frac{1}{2}\right)^{N_1} + \left(\frac{1}{2}\right)^{N_2} = \left(\frac{1}{2}\right)^{3} + \left(\frac{1}{2}\right)^{3}$$

$$= 0.125 + 0.125 = \frac{1}{8} + \frac{1}{8}$$

$$= 0.25 = \frac{1}{4}$$

An Example with Numbers

A population has had a population bottleneck of 4 for one generation, and there after has a very large (infinite) population size.

What is the total inbreeding coefficient (F_{IT}) for an individual that is the product of brother sister mating in this population?

F_{ST} = drift inbreeding = 1/8

F_{IS} = pedigree inbreeding = 1/4

F_{IT} = Total inbreeding = 0.34375

$(1-F_{IT}) = (1-F_{IS})(1-F_{ST})$

$F_{IT} = F_{IS} + F_{ST}(1-F_{IS})$

$F_{IT} = F_{ST} + F_{IS}(1-F_{ST})$

$(1-F_{IT}) = (1-1/4)(1-1/8) = 0.65625$

$= (1- 0.34375)$

$F_{IT} = 1/4 + 1/8(1-1/4) = 0.34375$

$F_{IT} = 1/8 + 1/4(1-1/8) = 0.34375$