

COI Bootcamp

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 August 17, 2015  [carol beuchat](#)  [Edit](#)

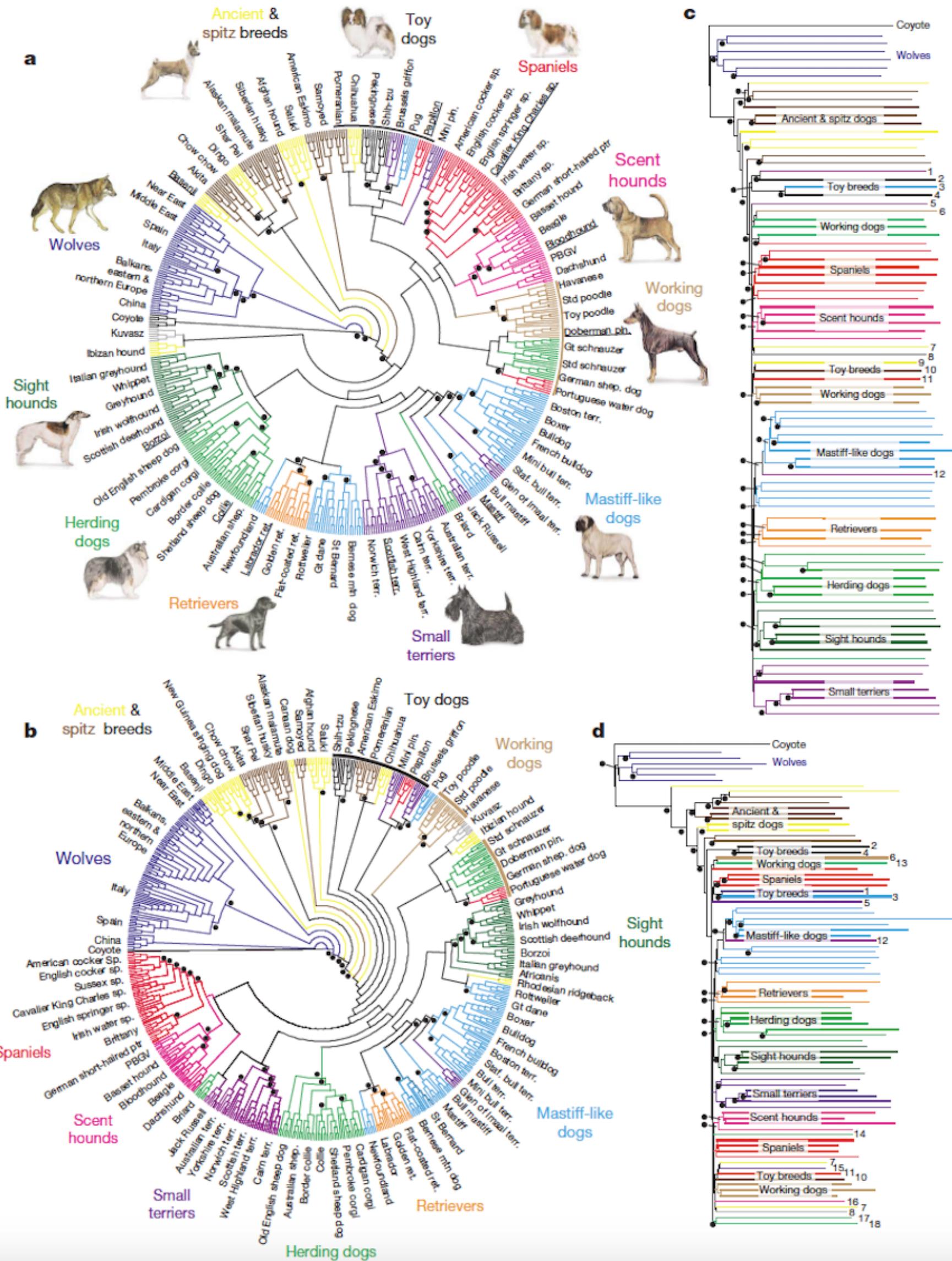
The good and bad of inbreeding

Carol Beuchat PhD & Pieter Oliehoek PhD

Institute of Canine Biology

Welcome to ICB's Coefficient of Inbreeding Bootcamp! You are going to learn about some very powerful tools that will make it easier for you to achieve your goals as a breeder, while at the same time reducing problems with genetic diseases. Many of you have probably heard of Coefficient of Inbreeding (COI), but few breeders know how to make the best possible use of it when designing a breeding program. Here we are going to give you a crash course on COI - what it means, how it is used, and why it will make you a better breeder.

Most of you probably know that the modern domestic dog shares ancestry with the wolf, and in fact the dog and wolf are now considered to be the same species. Starting with the rather non-descript phenotype (physical appearance) of the wolf, dog breeds have emerged with an astonishing variety of sizes, forms, shapes, colors, functions, and temperaments. But still, dogs and wolves are genetically similar enough to be considered a single species; wolf and dog differ by much less than 1% genetically, and the genetic differences among dog breeds are even smaller. Somehow, by mixing and matching just a relative handful of genes, breeders have been able to create the most physically diverse vertebrate on the planet.



(Figure from VonHoldt et al 2010, Genome-wide SNP and haplotype analyses reveal a rich history underlying dog domestication. Nature 464; doi:10.1038/nature08837)

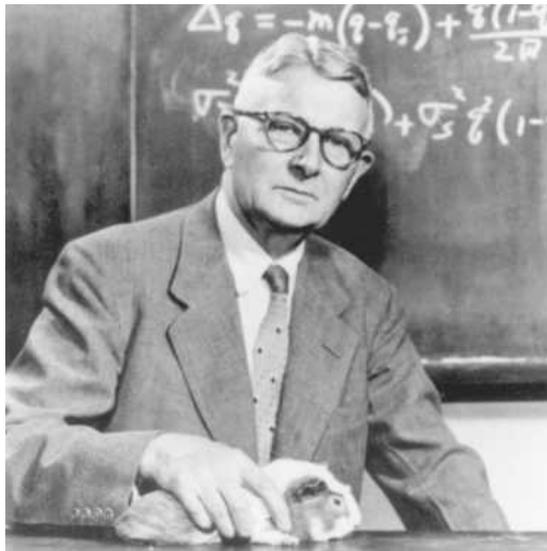
We are just beginning to understand the genetics of the dog, and the purebred dog has turned out to be an outstanding model animal in which to study many genetic disorders. While a boon to researchers, this is unfortunate for dogs. Over the generations, purebred dog breeds have been accumulating genes that result in inheritable disorders, and in many breeds the incidence of specific diseases is quite high. These breeds make good research models, but the negative impact on health and welfare is very real and of great concern.

Why are there so many genetic diseases in dogs? There is no mystery here: inbreeding in a closed gene pool increases genetic homozygosity, and homozygosity results in increased expression of traits caused by recessive alleles. A substantial fraction of the genetic disorders that plague dogs are caused by homozygous recessive mutations. This is both predictable and unfortunate.

If we understand why inbreeding is resulting in higher rates of genetic disorders, we should be able to do something about it. That's what we're going to learn about here.

Where did the Coefficient of Inbreeding come from and why?

First, a little history. The COI was "invented" by Sewall Wright, who was an evolutionary geneticist. He held various academic positions over the course of his career, and although he was more interested in theory than cattle and corn breeding, he was also employed by the US Department of Agriculture to bring "modern" genetics to animal breeding.



While Wright was at the USDA, he wrote a short but seminal paper about inbreeding in animals called "Coefficients of Inbreeding and Relationship" (1921), in which he describes the derivation of his new coefficient of inbreeding, "Wright's F". You will understand COI

better if you understand the problems Wright was trying to solve when he did this.

Even in the 1920's, it was well known that inbreeding produced two effects (Wright 1921):

"First, a decline in all elements of vigor, as weight, fertility, vitality, etc., and second, an increase in uniformity within the inbred stock, correlated with which is an increase in prepotency in outside crosses."

"The best explanation of the decrease in vigor is dependent on the view that Mendelian factors unfavorable to vigor in any respect are more frequently recessive than dominant, a situation which is the logical consequence of the two propositions that mutations are more likely to injure than improve the complex adjustments within an organism and that injurious dominant mutations will be relatively promptly weeded out, leaving the recessive ones to accumulate, especially if they happen to be linked with favorable dominant factors. On this view, it may be readily shown that the decrease in vigor in starting inbreeding in a previously random-bred stock should be directly proportional to the increase in the percentage of homozygosity."

"As for the other effects of inbreeding, fixation of characters and increased prepotency, these are of course in direct proportion to the percentage of homozygosity. Thus, if we can calculate the percentage of homozygosity which would follow on the average from a given system of mating, we can at once form the most natural coefficient of inbreeding."

The Good and Bad of Inbreeding

What are the potential effects of inbreeding that Wright was interested in? They include:

ADVANTAGES

- › *increased uniformity*
- › *increased prepotency (ability to pass on traits to offspring)*
- › *"fixing" of desired traits and breed type*

DISADVANTAGES

- › *lower fertility*
 - › *lower "vigor"*
 - › *birth defects*
 - › *smaller size*
 - › *fewer offspring*
 - › *slower growth*
 - › *higher offspring mortality*
 - › *shorter lifespan*
 - › *increase in genetic diseases*
 - › *reduced "genetic potential" (ability to improve a trait)*
-

On the left, the "advantages", are the benefits breeders want to achieve. On the right are the negative consequences that breeders would like to avoid. Clearly, while breeders want to use inbreeding to improve their breeding program, they also risk any of a long list of harms that can be very damaging to their animals, in both the short term and long. We will be talking more about this later.

Animals in closed populations

Most animals in the wild avoid mating with relatives if possible. It does happen in some animals, or under certain conditions, but in general animals can detect kin and degree of relatedness and they avoid inbreeding. When populations are isolated or closed because of geography (e.g., islands, landscapes with physical barriers to movement like mountains or deserts), the regular movements of animals between groups that would increase gene flow are reduced or prevented entirely. These are genetically "closed" populations, and inbreeding cannot be avoided. So inbreeding in the population increases and genetic diversity decreases unavoidably over time, and the smaller the population the more rapidly it increases.

A population can be quite large, but if the number of animals that actually breed is small, the "effective population size" will have a profound effect on the rate of inbreeding. Purebred dogs are by definition closed populations - gene flow into the population is prohibited by a closed stud book (the record of registrations). In effect, ALL breeding in purebred dogs is inbreeding. After starting with a number of dogs that are the first registered members of their breed (the "founders"), the studbook is subsequently closed. Every animal in the population is related, so breeders can ONLY inbreed. Inbreeding increases over time, and more quickly if only a fraction of the adult animals are bred.

This is illustrated in these figures from the [program](#) for sustainable breeding of native Nordic dog breeds initiated by NordGen in collaboration with researchers in Denmark, Norway, Finland, and Iceland. Effective population sizes of many breeds are less than 100, and too many are only a fraction of that. Anything less than about 50 is considered to be a population at risk of extinction.

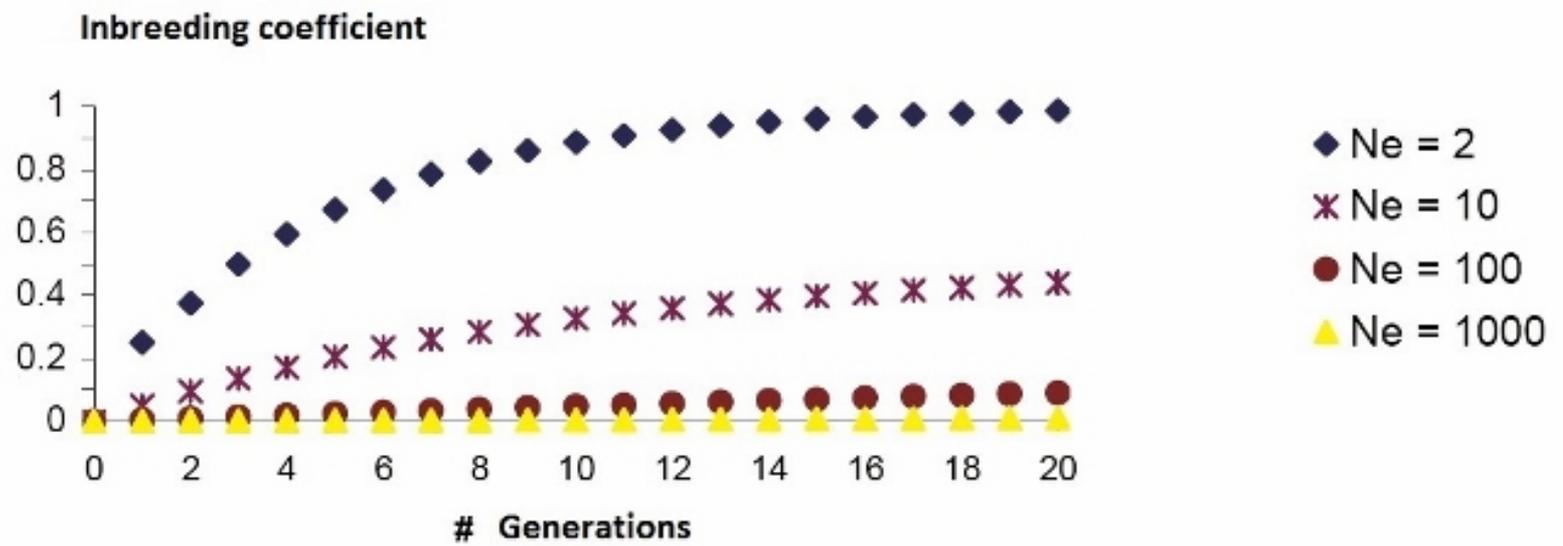


Figure 1: Inbreeding coefficient as a function of the number of generations for different effective population sizes (N_e).

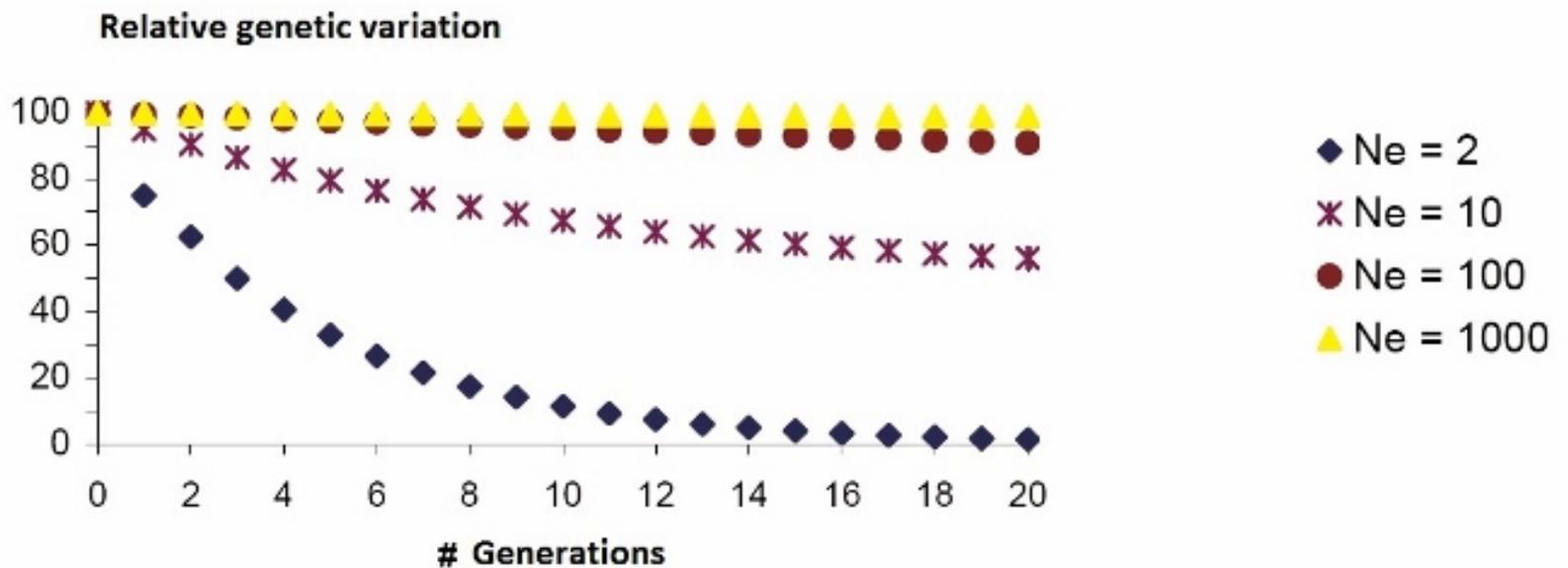


Figure 2: Relative amount of genetic variation in a population as a function of number of generations for different effective population sizes (N_e).

So under the current system of closed stud books for pedigreed dogs, inbreeding is essentially required by the definition of "pure-bred". But the advantages and disadvantages of inbreeding apply to dogs just as they do to any other animal. Uniformity and the ability to reliably pass on specific traits of a breed to the next generation increase over time, but so do infertility, offspring mortality, lifespan, and inherited genetic diseases. Animals in closed populations eventually, inevitably go extinct as the quality of the gene pool declines. But inbreeding can be managed by breeders who consider the health of the gene pool as well as the quality of the next litter in their breeding plans. Damaged gene pools can be repaired and improved, genetic disorders can be reduced, and many of the negative consequences of inbreeding can be controlled - if breeders adopt appropriate breeding strategies. We are going to show you how to use COI and other tools from population genetics to do this.

The Genetics of Inbreeding

We're going to dig deep into inbreeding, so it will be useful for us to review some of the basic genetic concepts so we can all be on the same page when we start.

We have for you a nice video produced by the [Khan Academy](#). The perspective is from human biology, but all of it applies to any other populations of animals including dogs. An important point to note is that most of the hundreds of genetic disorders in dogs are caused by autosomal recessive mutations. This is the same mode of inheritance as Tay Sacs disease, which is used as an example for humans in the video, so the application to breeding dogs is clear.

VIDEO 1: <https://youtu.be/eg7ltl5vll0>



Khan Academy - Inbreeding: Learn about inbreeding and how it can hurt a population's genetic diversity. By Ross Firestone.

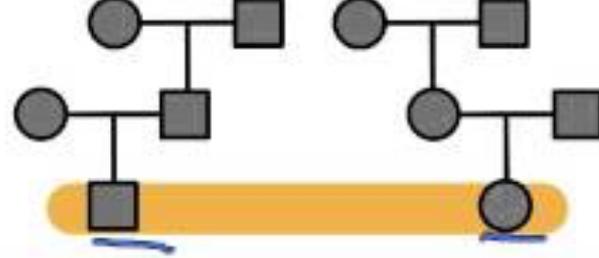
After that general introduction, we can start thinking about inheritance of specific alleles, the relationship between relatedness and genetic similarity, and what is meant by "identical by descent". What is the genetic similarity between siblings? What about cousins? What can we learn by looking at pedigree relationships?

VIDEO 2: <https://youtu.be/c0XLN6eKvMk>

A YouTube video player thumbnail for a video titled "Lecture 8C - Inbreeding". The main title of the video is "Actual identity by descent between second cousins." The thumbnail includes a play button icon in the center. On the left side, there is a list of video titles, with "Second-cousin pair A" highlighted. On the right side, there is a small pedigree diagram showing a couple (represented by a circle and a square) with two children (represented by a circle and a square). Below the diagram, text reads: "The blue bars show the identical segments between two different pairs of second cousins." The video player interface also shows a clock icon and a share icon in the top right corner.



Second-cousin pair B



CeCe Moore, with permission: <http://www.yourgeneticgenealogist.com/2011/05/known-relative-studies-with-23andme.html>

9

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If you're interested, you can read more about the example of the Israeli Samaritans that was mentioned in this video [HERE](#).

In the next section, we will introduce a definition of "inbreeding" that is specific to our discussion of COI, and we will use a dog pedigree to work through how the inbreeding coefficient is calculated.

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COI Basics

You'll need to correctly answer at least **14 of the 19** questions below (**at least 70%**) to progress to the next unit.

Question #1 - Some of the questions are easy, some you might not be able to answer correctly the first time. But nobody fails here :-) - we want you to look at the ones you missed, review the material for the lesson, and try again. We don't care how many times you have to try, and we don't even care if you look at the lesson while taking the test. Memorization isn't the point; it's understanding. So, take your time, and think carefully. When you're ready, just mark this "question" TRUE, and off you go!

- > True
 - > False
-

Question #2 - The coefficient of inbreeding has been used in animal breeding for more than 75 years.

- > True
 - > False
-

Question #3 - Inbreeding has both advantages and disadvantages.

- > True
 - > False
-

Question #4 - Homozygosity increases prepotency in outcrosses.

- › True
 - › False
-

Question #5 - Most of the genes that cause reduced vigor and vitality (inbreeding depression) are dominant.

- › True
 - › False
-

Question #6 - Dominant mutations tend to accumulate in a population of animals over time.

- › True
 - › False
-

Question #7 - Recessive mutations tend to accumulate in a population of animals over time.

- › True
 - › False
-

Question #8 - Inbreeding increases fertility.

- › True
 - › False
-

Question #9 - Wright's coefficient of inbreeding is an estimate of

- › lifespan
 - › homozygosity
 - › number of mutations
-

Question #10 - Animals that are more inbred have greater heterozygosity.

- › True
 - › False
-

Question #11 - An animal with two copies of the same allele at a locus is homozygous for that gene.

- › True

> False

Question #12 - Mutations are caused by inbreeding.

- > True
 - > False
-

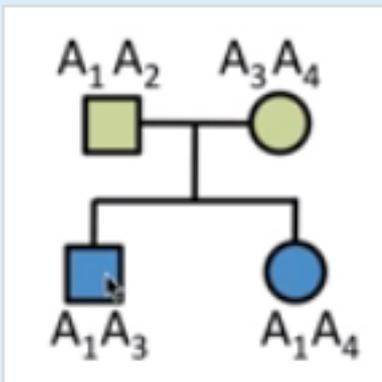
Question #13 - If two siblings have the same allele at a particular locus and they got it from a common ancestor, that is called

- > identical by descent.
 - > genetic descent.
 - > homozygosity.
 - > cloning.
-

Question #14 - Dogs inherit more of their genes from the sire than the dam.

- > True
 - > False
-

Question #15 - This mating produced offspring with the alleles A1-A3 and A1-A4 at a particular locus. But the mating would be just as likely to produce offspring that are A1-A3 and A1-A3; that is, both offspring have the same alleles for that locus.



- > True
 - > False
-

Question #16 - What is the genetic similarity between a parent and child?

- > 75%
 - > 50%
 - > 25%
 - > 12.5%
 - > because of probability, you can't know for sure.
-

Question #17 - What is the genetic similarity between two full siblings?

- › 75%
 - › 50%
 - › 25%
 - › 12.5%
 - › because of probability, you can't know for sure.
-

Question #18 - Healthy animals have very few deleterious alleles in their genomes.

- › True
 - › False
-

Question #19 - The relatedness of two animals is the same as their inbreeding.

- › True
 - › False
-

[Next Unit »](#)

🕒 August 14, 2015 👤 carol beuchat ✎ Edit

Inbreeding & relatedness

If we're going to learn about inbreeding, we need to understand what it is. In this video, Dr Pieter Oliehoek discusses the meanings of the words "inbreeding" and "relatedness", and how they apply to discussions about the breeding of dogs.

VIDEO: <https://youtu.be/6A235Y1RkII>

Inbreeding:
Breeding of animals from which
the parents are related

Share common ancestors!

WOM, BAB...
THERE'S SOMETHING
YOU NEED TO KNOW --
IN A PARVALE!

The screenshot shows a video player interface. The title bar reads "Inbreeding - being related" and "Lesson 2 - ICB Boot Camp". The video content is split into two panels. The left panel contains text defining inbreeding and a cartoon of dinosaurs. One dinosaur says, "WOM, BAB... THERE'S SOMETHING YOU NEED TO KNOW -- IN A PARVALE!". The right panel shows a man speaking and a still image of Noah's Ark.

Dr Pieter Oliehoek is a quantitative and population geneticist with a PhD from Wageningen University (The Netherlands). He is involved in management of breeding programs of both endangered species and rare domestic breeds, as well as dogs. He has had Icelandic Sheepdogs since his youth, and did a seminal study of the population genetics of the breed for his doctoral thesis.

You can read more about his work on Icelandic Sheepdogs here:

[What population genetics can tell you about a breed: the Icelandic Sheepdog](#)

You'll need to correctly answer at least **5 of the 7** questions below (**at least 70%**) to progress to the next unit.

Question #1 - Dogs that are inbred should not be used for breeding because their offspring will be inbred as well.

- > True
 - > False
-

Question #2 - In population genetics, the "founders" of a breed are assumed to be unrelated.

- > True
 - > False
-

Question #3 - The founders of a population are

- > the first male and female of the population
 - > the group of unrelated animals from which all animals in the population are descended.
 - > unrelated to the current breeding population.
-

Question #4 - We can talk about Inbreeding as a property of an individual animal.

- > True
 - > False
-

Question #5 - We can talk about inbreeding as a property of a population.

- > True
 - > False
-

Question #6 - Which of these is LEAST important in producing variation in a dog breed?

- > mutation
 - > selection
 - > genetic drift
-

Question #7 - Which is the best definition of inbreeding to use when considering populations or breeds of purebred dogs?

- > Inbreeding is the breeding of animals that are related
 - > Inbreeding is the breeding of animals that produce offspring that are more related than average.
-

[« Previous Unit](#)

[Next Unit »](#)

🕒 August 14, 2015

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Determining the inbreeding coefficient

Defining COI

In this course, we are using a special definition of inbreeding, using the context of COI:

“ **Inbreeding coefficient of an individual is the probability that both alleles at a randomly taken locus of this individual are identical by descent.**

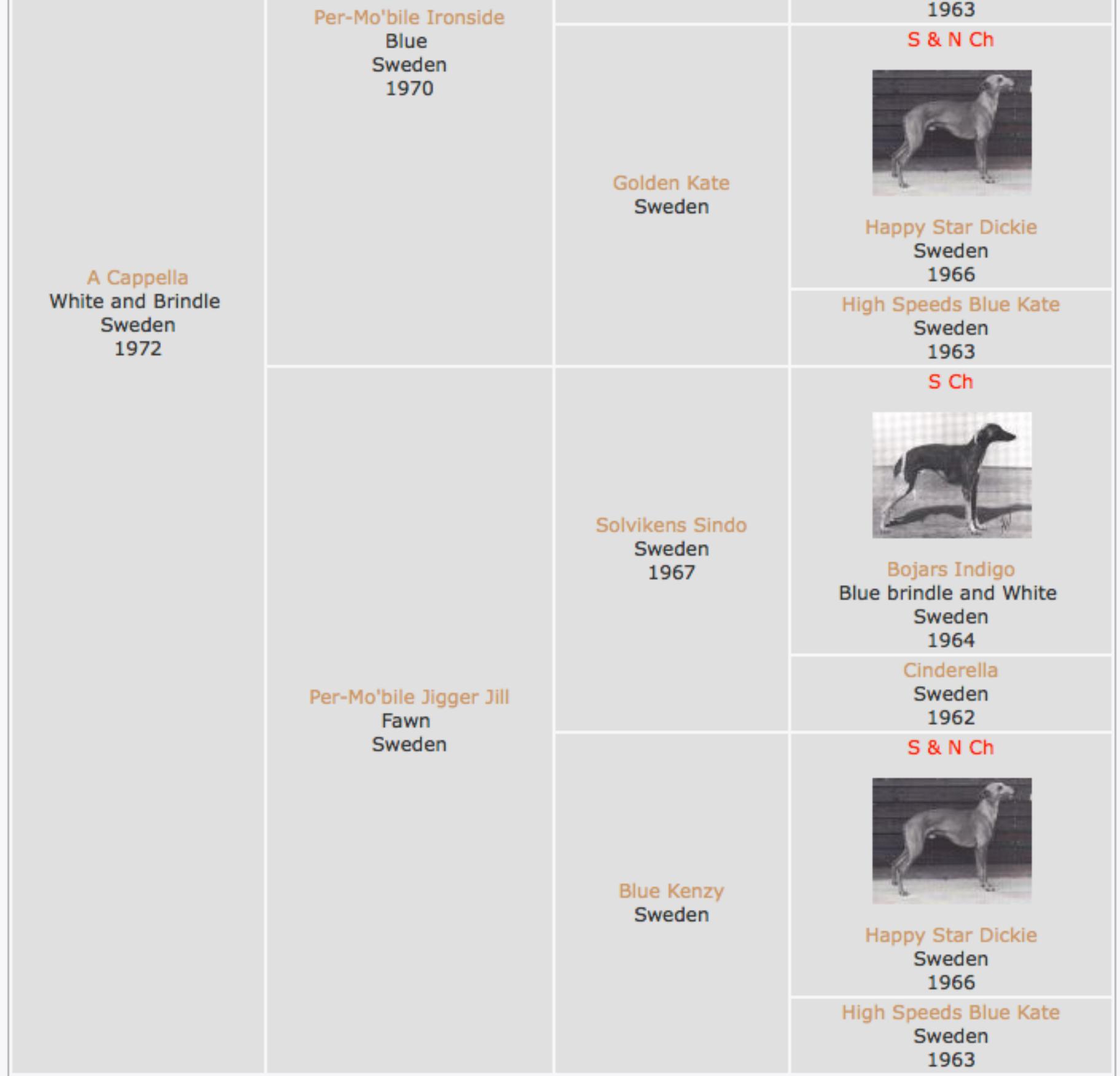
Or in other words: the average homozygosity in an animal that is caused by ancestors common to both the sire and dam.

An animal inherits one copy of every gene from both its sire and dam. There can be many different versions of a gene (these are called alleles), but each animal can have at most two. If the pair of alleles in an animal are exactly the same version of the gene, that gene is "homozygous" (e.g., AA or aa); if the alleles are different, that gene is heterozygous (e.g., Aa). If the sire and dam share a common ancestor, they might both have a copy of a particular allele that originated in that common ancestor, and therefore one of their offspring could inherit that same allele from both parents.

Let's look at a pedigree

Here is a standard 3 generation pedigree of a whippet born in 1972. This has some inbreeding that originates in the third generation, specifically *A Cappella's* two grandmothers were full siblings (Golden Kate and Blue Kenzy); they were offspring of Happy Star Dickie x High Speeds Blue Kate.





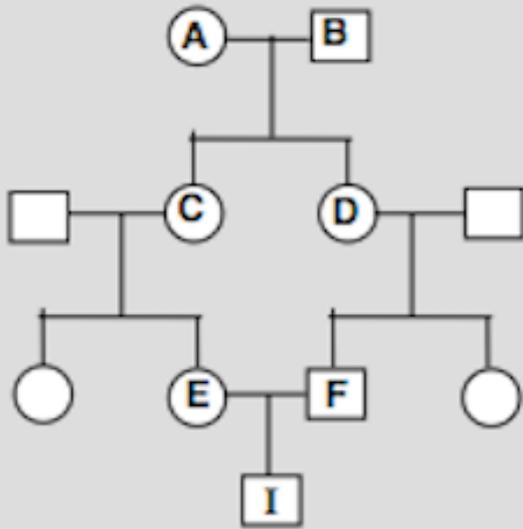
Let's explore the inbreeding in this pedigree. First, we can simplify it by re-drawing this way:

Our dog *A Cappella* is at the bottom ("I"), the shared great-grandparents are at the top ("A" and "B"), and we can leave off the rest of the dogs.

We can see that if A has a copy of an allele for a particular gene (let's call it *Ta*), A could have passed it to C, then C to E, then E to *A Cappella* (I); similarly, A could have passed the *Ta* allele to D, who passed it to F, and then to *A Cappella*.

If this happened, then *A Cappella* would be homozygous for the *Ta* allele. In fact, we would say that *A Cappella* was "homozygous by descent" for that gene, which means that the two *Ta* alleles are not only identical, but they also originated from an ancestor that occurs on both the dam's and the sire's sides of the pedigree. (A gene can also be "homozygous by state", which means the alleles are identical, but they did not originate from an ancestor that appears on both sides of the pedigree.)

Conventional representation



We have described the paths an allele belonging to A could take to end up in *A Cappella* (I). But there is another ancestor of *A Cappella* that is on both sides of the pedigree, which is B. We could similarly trace the path an allele (let's say Tb) could take to get from B to *A Cappella* - B to D to F to I, and also B to C to E to I.

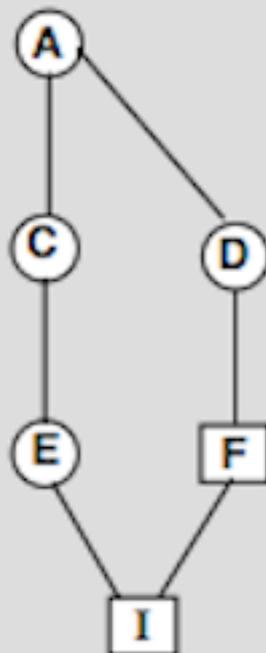
So we can see how an allele originating from one of the great grandparents (A or B) could show up in their descendant *A Cappella*. And we can see how *A Cappella* might end up with two identical copies of that allele, one each from her two parents E and F, making her homozygous (and identical by descent) for that allele.

But how likely is this to happen? We know that each gene in an animal has two alleles, which can be different or identical (e.g., TaTa, or TaTb; homozygous or heterozygous). Which of the two alleles gets passed to the offspring is (theoretically) random, so in a litter of puppies, some will get Ta and some will get Tb if the parent is heterozygous. Therefore, the

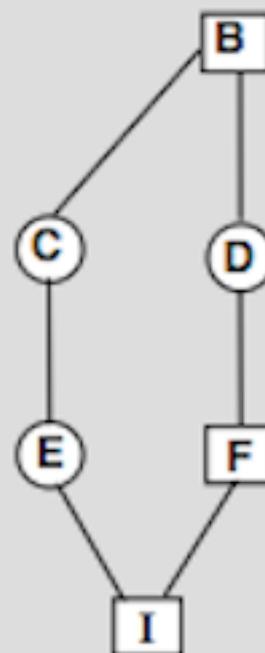
probability of getting a particular allele is one chance in two, or $1/2 = 0.5$, or 50%.

If we start with A, the probability of allele Tb being passed to offspring C is 50%. Likewise, the chance of the Tb allele being passed from C to E is also 50%; and from E to I, also 50%. We have a series of steps, each with a probability of 50%. The probability that the Tb allele in A will be inherited through the series of ancestors C and E by the dog I is the product of the individual probabilities of each step, which are all 0.5. And the allele Tb can be similarly passed on to I via the other side of the pedigree, through D and F.

Path 1



Path 2



Knowing that the probability of the allele moving from an ancestor to a descendent is 0.5, we can calculate the probability of moving from an ancestor through multiple descendants by multiplying the individual probabilities for each step.

So, for an allele to be passed down the left branch of Path 1 from ancestor A to descendant I (above), we would calculate the probabilities like this:

$$\text{for } A \rightarrow C, p = 0.5 \text{ (or 50\%)}$$

$$\text{for } A \rightarrow E, p = 0.5 \times 0.5 = 0.25 \text{ (or 25\%)}$$

$$\text{for } A \rightarrow I, p = 0.5 \times 0.5 \times 0.5 = 0.125 \text{ (or 12.5\%)}$$

Now, what do we do to determine the probability of I inheriting two copies of the same allele from ancestor A? We need to consider the probabilities for each of the steps through the right branch of Path 1; i.e., A to D to F to I.

An easy way to do this calculation is by determining the number of ancestors in path starting from I (at the bottom) and counting each animal (node) to complete the loop through A and down the opposite side of the path. So for Path 1 above starting at I, that would be

$$\rightarrow E \rightarrow C \rightarrow A \rightarrow D \rightarrow F$$

There are 5 animals in this complete path (from I back to I), and we know the probability of a particular allele being transmitted at each step is 0.5, so we can calculate the total probability as

$$F = (0.5) \times (0.5) \times (0.5) \times (0.5) \times (0.5), \text{ or } = (0.5)^5$$

$$\rightarrow \text{or, } F = 0.03125 \text{ (3.1\%).}$$

The "F" here is **Wright's F** - the Coefficient of Inbreeding (COI).

The calculation we just did indicated that there is just a 3% chance that I will be homozygous for an allele that originated in ancestor A. Likewise, because of the inbreeding with A, about 3% of the genome of I will be homozygous.

So, for the next step, we have to consider both parents involved in this inbreeding, A and B in the first stick-figure pedigree diagram above. The paths for B are just the same for A, so once again we have 5 animal nodes, and the F we would calculate due to inbreeding from B is once again 3.1%.

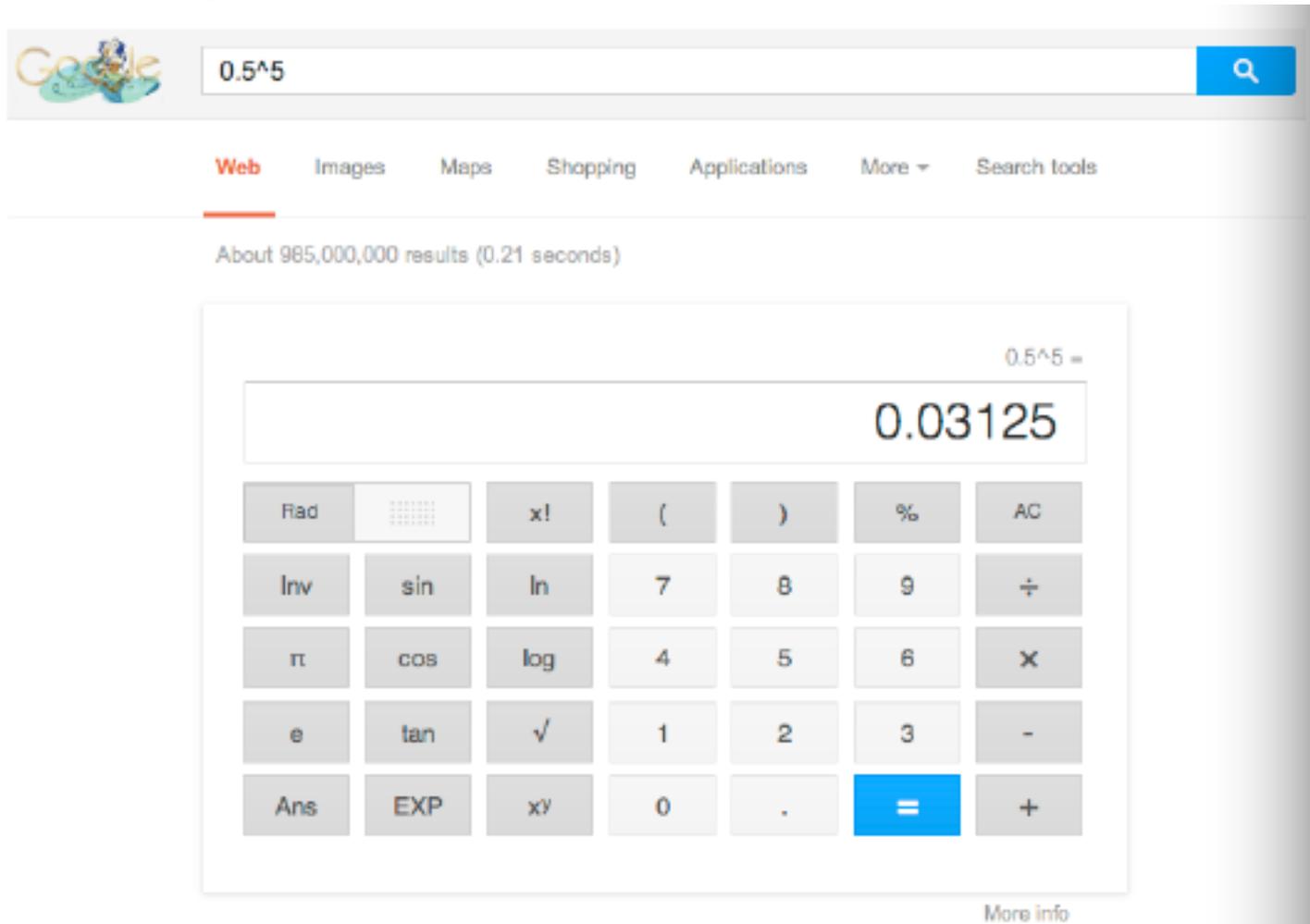
Now finally, we can compute the total probability of homozygosity in this breeding as

$$\rightarrow F = 3.125\% + 3.125\% = 6.25\%;$$

\rightarrow therefore the COI of animal I is 6.25%.

Going back to the whippet pedigree above, the COI we would calculate for *A Capella* from the pedigree as we see it here is 6.25%. This probability is exactly the same for a "good" gene (eg great temperament, coat color) as for a bad one (PRA, blue nose). Which genes she will be homozygous for is a crap shoot; you can't breed for uniformity and predictability in some traits without also paying a penalty for increased homozygosity - and this, you'll recall from the first lesson, is the reason Wright derived the inbreeding coefficient in the first place. We won't gain a huge amount of homozygosity in the alleles we want if the coefficient of inbreeding is low (e.g., 6.25%), but then we are also keeping the level of risk relatively low - the probability of producing a dog that is homozygous for a gene we DON'T want is only 6.25%. At COI of 6.25%, we accept a modest level benefit for a tolerably low level of risk.

This is a good place to stop so you can practice working out the paths in a few pedigrees and computing the inbreeding coefficients. Things to remember - the focal animal (in these examples, individual I) - doesn't count as an animal in the loop. Start with that animal and count the number of animals in a loop through the common ancestor and back again (call this "n"). Then calculate F (the coefficient of inbreeding) as 0.5 multiplied by 0.5 "n" times, or 0.5 raised to the power "n". You don't need a fancy calculator to do this - let Google do the work! Just type the formula into the Google search bar (use the "up" carrot ^ (shift 6) for the superscript), and Google will come back with a digital calculator with your answer.

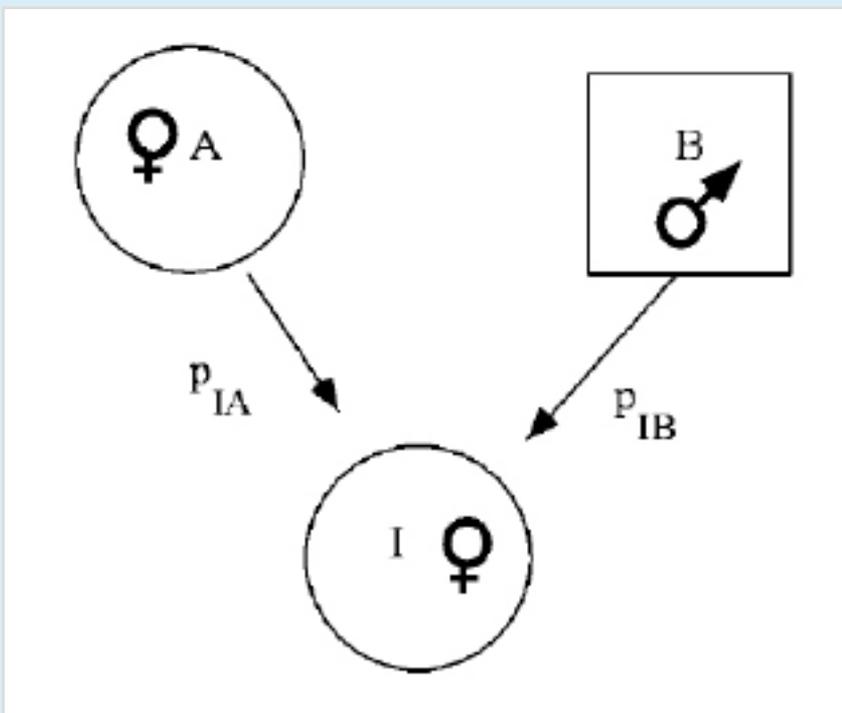


The image shows a Google search interface. The search bar contains the text "0.5^5". Below the search bar, there are navigation tabs for "Web", "Images", "Maps", "Shopping", "Applications", "More", and "Search tools". The search results show "About 985,000,000 results (0.21 seconds)". A digital calculator is displayed, showing the calculation "0.5^5 =" and the result "0.03125". The calculator interface includes various mathematical functions like Rad, Inv, π, e, Ans, EXP, x!, (,), %, AC, sin, ln, 7, 8, 9, ÷, cos, log, 4, 5, 6, ×, tan, √, 1, 2, 3, -, and a grid of numbers 0-9, a decimal point, and an equals sign.

Calculating COI

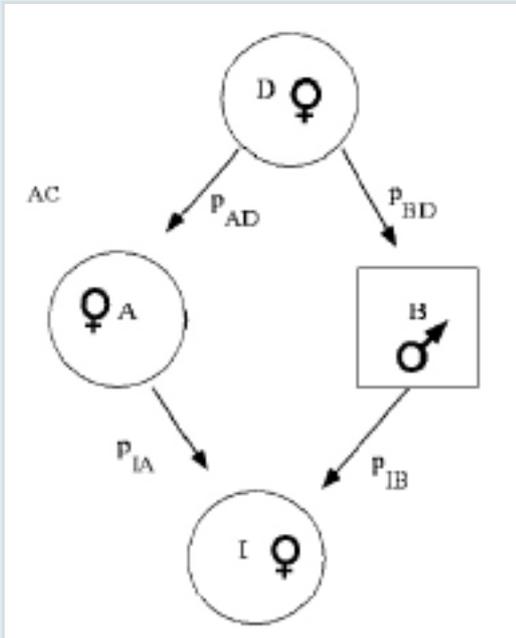
You'll need to correctly answer at least **6 of the 8** questions below (**at least 70%**) to progress to the next unit.

Question #1 - What is the coefficient of inbreeding of animal I?



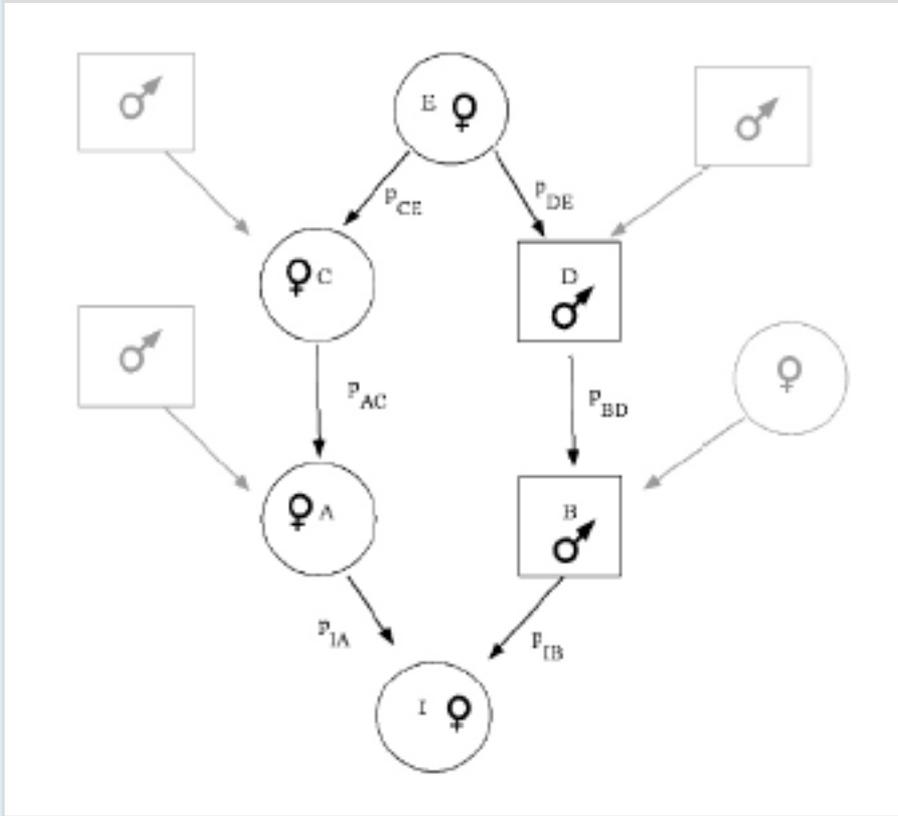
- > 0%
- > 3.1%
- > 6.25%
- > 12.5%
- > 25%
- > 50%

Question #2 - What is the coefficient of inbreeding of animal I?



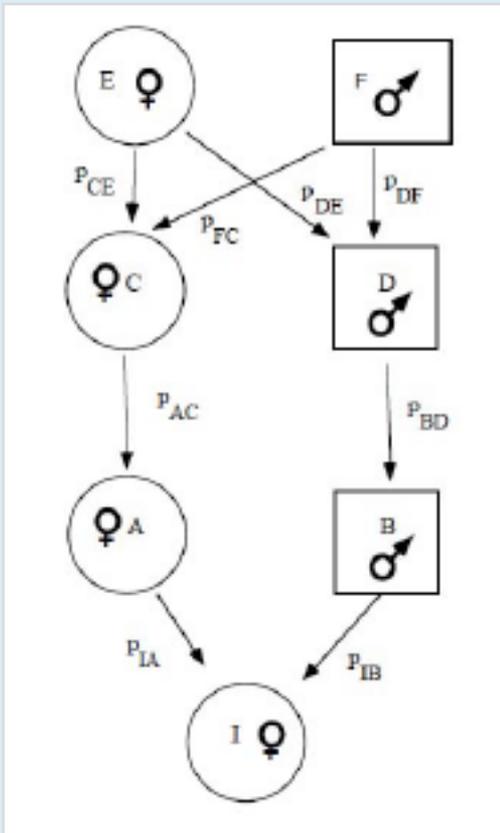
- > 0%
- > 3.1%
- > 6.25%
- > 12.5%
- > 25%
- > 50%

Question #3 - What is the coefficient of inbreeding of animal I?



- > 0%
- > 3.1%
- > 6.25%
- > 12.5%
- > 25%
- > 50%

Question #4 - What is the coefficient of inbreeding of animal I?



- > 0%
- > 3.1%
- > 6.25%

> 12.5

Question #5 - Alleles that are homozygous by descent were inherited from the same ancestor down both the maternal and paternal lines.

- > True
 - > False
-

Question #6 - Let's say a sire has two alleles at a locus, B1 and B2. What is the probability that his daughter will inherit B2?

- > 0%
 - > 3.1%
 - > 5%
 - > 6.25%
 - > 12.5%
 - > 50%
-

Question #7 - Let's say a sire has two alleles at a locus, B1 and B2. What is the probability that his grand-daughter will inherit B2?

- > 0%
 - > 3.1%
 - > 5%
 - > 6.25%
 - > 12.5%
 - > 25%
 - > 50%
-

Question #8 - Let's say a sire has two alleles at a locus, B1 and B2. What is the probability that his great-granddaughter will inherit B2?

- > 0%
 - > 3.1%
 - > 5%
 - > 6.25%
 - > 12.5%
 - > 25%
 - > 50%
-

Pedigree Structure & COI

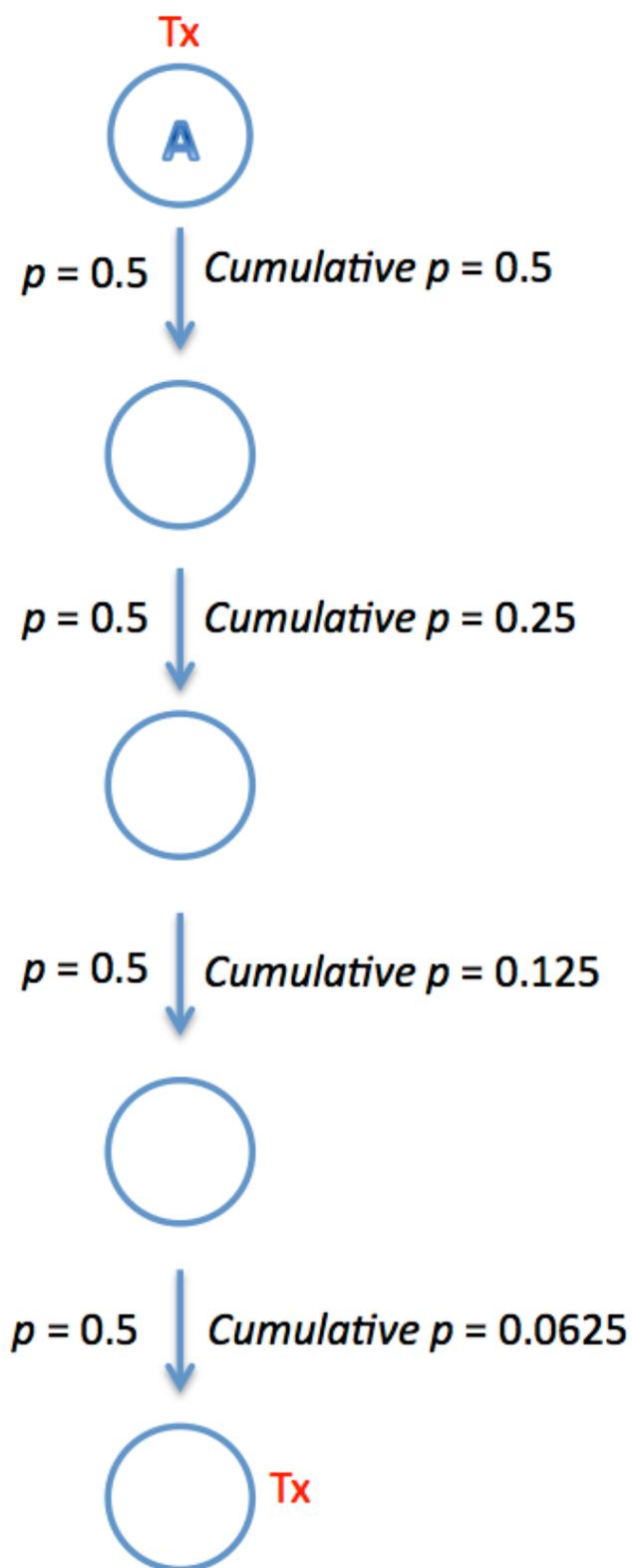
Each parent passes only one of two possible alleles on to an offspring, with a probability of 0.5 for each. When you diagram a pedigree, this 0.5 probability of inheritance must be accounted for at each generation. So, with each passing generation, the cumulative probability of a specific allele from an ancestor passing to the next goes down by half.

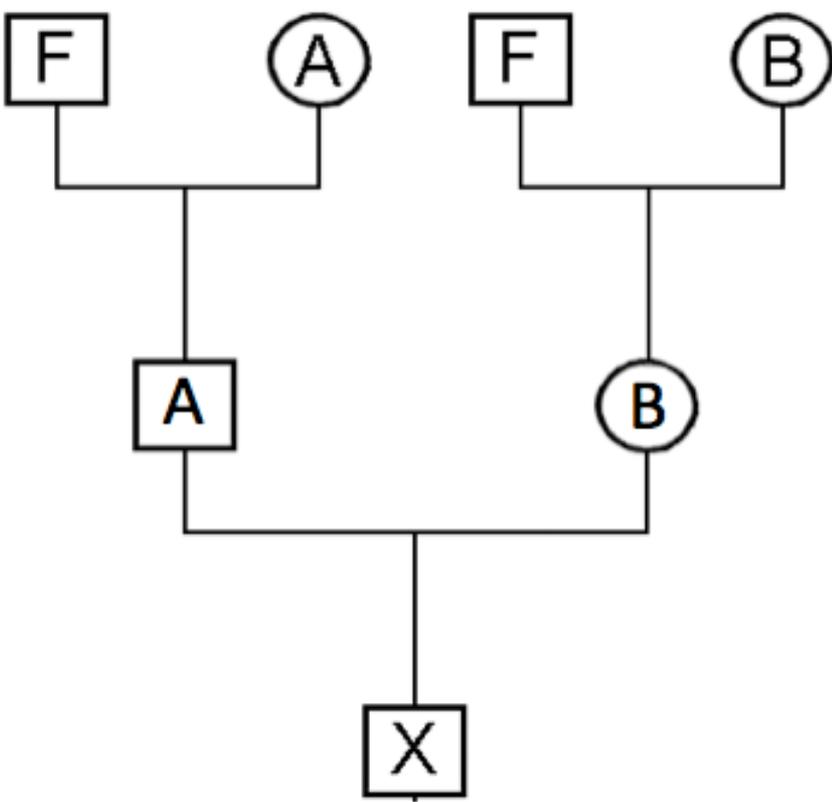
For this reason, when considering the likelihood of an animal inheriting two copies of the same allele from an ancestor, that ancestor's position in the pedigree is extremely important. The deeper an ancestor is in the pedigree, the lower the chance of inheriting an allele that originated with that animal.

The complication is that if an ancestor appears multiple times in a pedigree, as is common when there is inbreeding or line-breeding, each of those appearances must be accounted for in the calculation of the cumulative probability. As pedigrees become more complicated, it gets harder to mentally estimate the resulting coefficient of inbreeding for a descendant.

You can see how this works using the sample pedigrees below. For each, calculate the coefficient of inbreeding of animal X. The first pedigree is the simplest, and you will see that the other pedigrees copy this same pedigree structure in different combinations and positions. You will save some time if you recognize that once you figure out the COI for the first pedigree, you can "substitute" that value in the others anywhere the same arrangement occurs.

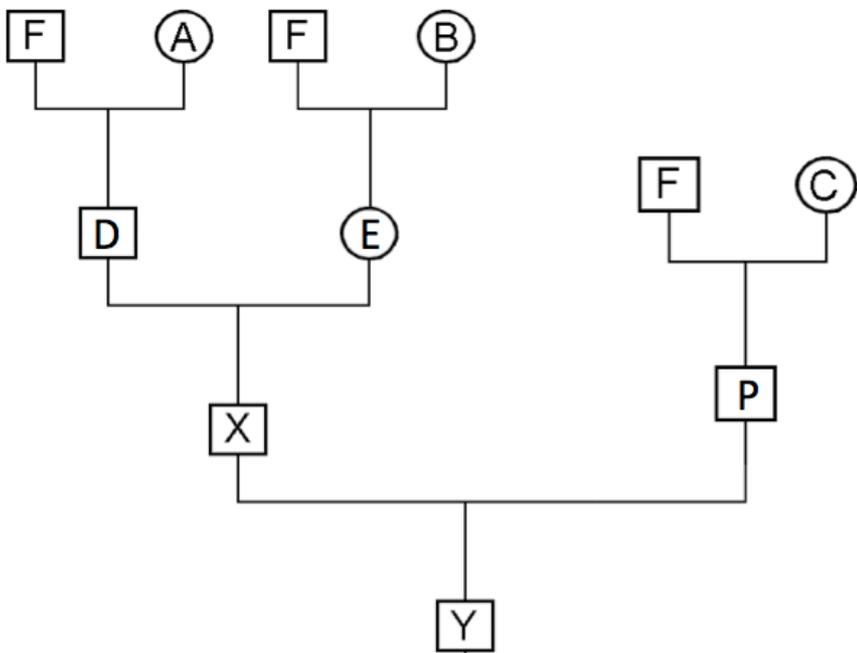
After you figure these out, mark your answers using the quiz that follows.





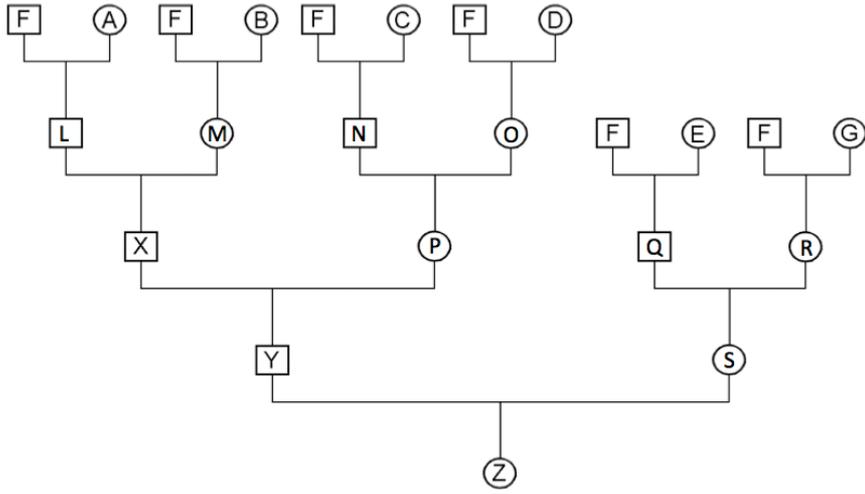
Pedigree #2

(click to enlarge)



Pedigree #3

(click to enlarge)



Pedigree Structure & COI

You'll need to correctly answer at least **3 of the 3** questions below (**at least 70%**) to progress to the next unit.

Question #1 - What is the COI of X in Pedigree #1?

- > 0.25
- > 0.125
- > 0.0625
- > 0.03125

Question #2 - What is the COI of Y in Pedigree #2?

- > 0.25
- > 0.125
- > 0.0625
- > 0.03125

Question #3 - What is the COI of Z in Pedigree #3?

- > 0.25
- > 0.125
- > 0.0625
- > 0.03125
- > 0.0156

Pedigree problems review

Pedigree problems review

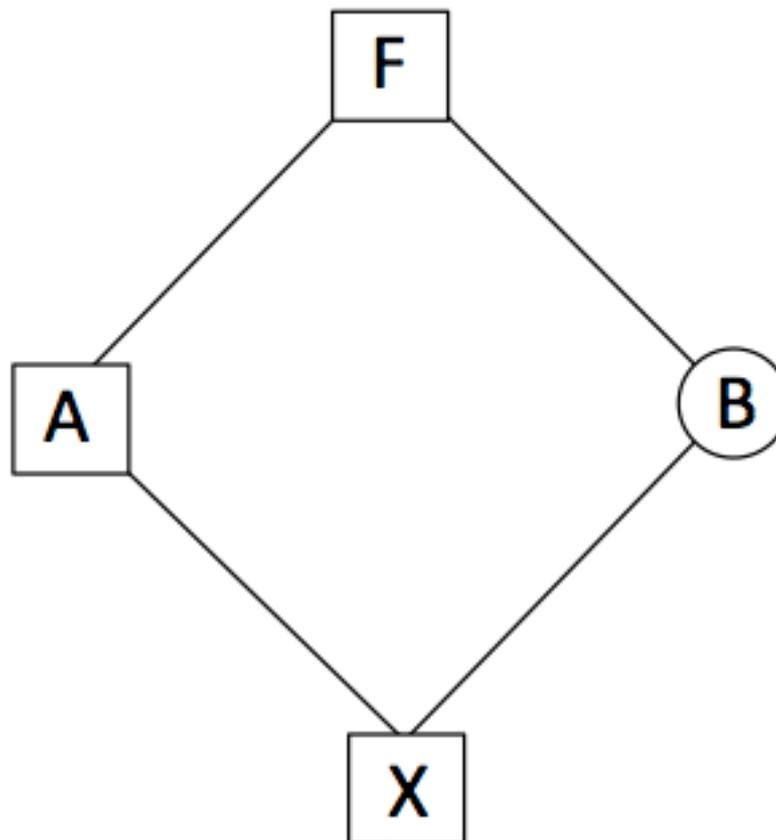
You had three pedigrees to work with in the previous lesson. Here's what you should have ended up with.

Pedigree #1

The paths go from X to: A-->F-->B

There are 3 animals in the path.

So $COI = (0.5 \times 0.5 \times 0.5) = 0.125$ (or 12.5%)



Pedigree #2

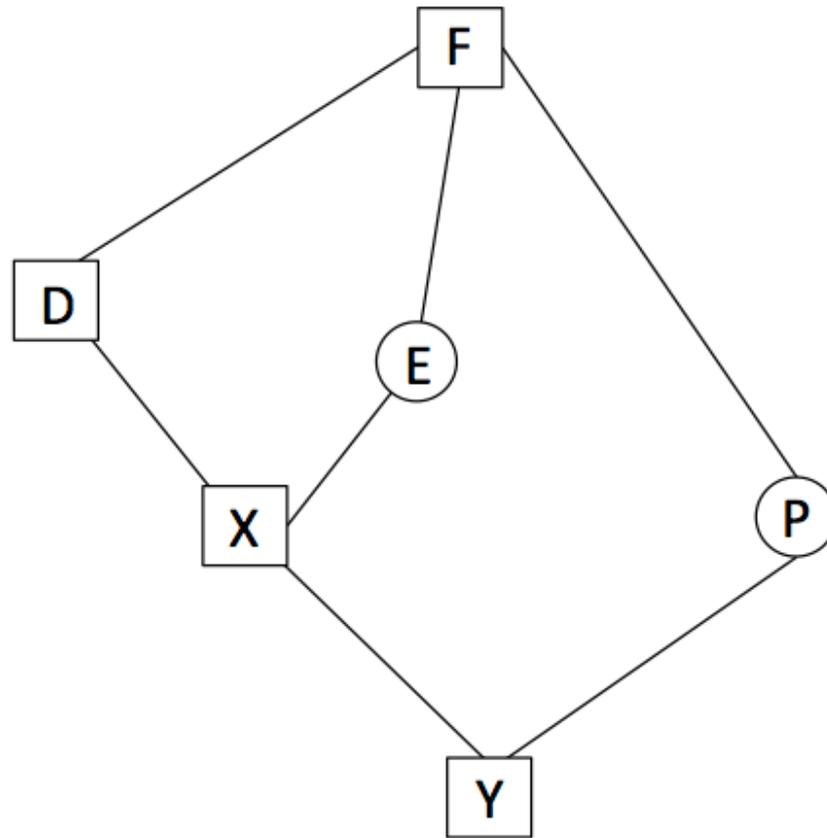
There are two paths from Y:

a) X-->D-->F-->P

b) X-->E-->F-->P

There are 4 animals in each path.

So COI = $(0.5 \times 0.5 \times 0.5 \times 0.5) \times 2 = 0.125$ (or 12.5%)



Pedigree #3

There are 8 paths from Y:

a) Y-->X-->L-->F-->R-->S

b) Y-->X-->L-->F-->Q-->S

c) Y-->X-->M-->F-->R-->S

d) Y-->X-->M-->F-->Q-->S

e) Y-->P-->N-->F-->R-->S

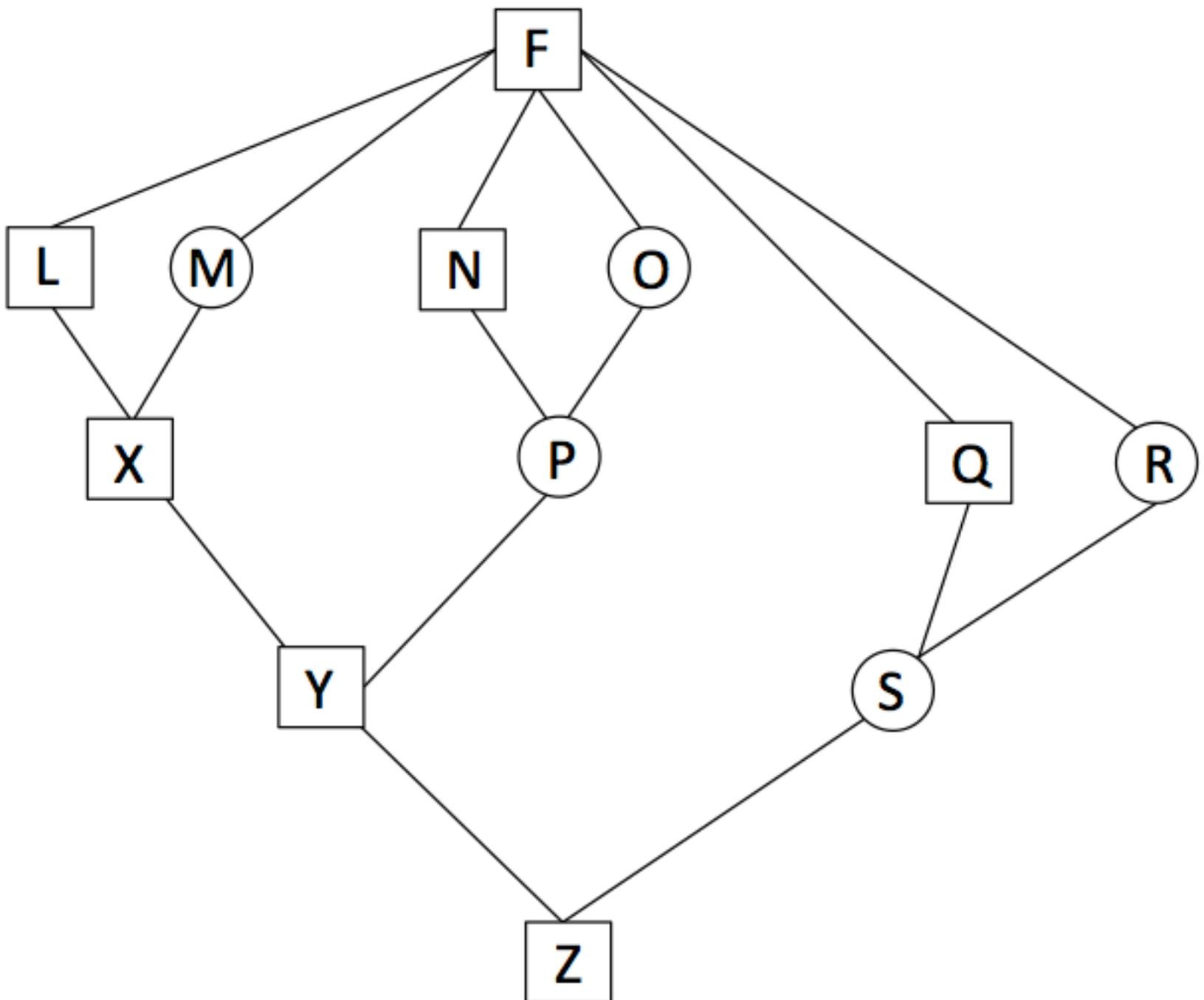
f) Y-->P-->N-->F-->Q-->S

g) Y-->P-->O-->F-->R-->S

h) Y-->P-->O-->F-->Q-->S

There are 6 animals in each path.

So COI = $(0.5 \times 0.5 \times 0.5 \times 0.5 \times 0.5 \times 0.5) \times 8 = 0.125$ (or 12.5%)



So here we have three pedigrees that are very different but have exactly the same coefficient of inbreeding for animal Z. This is because although the ancestor F appears 3 times in pedigree 2 and 6 times in pedigree 3, it is deeper in the pedigree, so there are additional steps in the paths that must be accounted for. I'm sure you can see that we could have continued to add generations with a

similar pattern, pushing F back farther in the pedigree, but we could still end up with the same COI.

And of course if you use a pedigree with too few generations in it so that F doesn't appear, the inbreeding coefficient you calculate for Z would be zero. All that would mean is that there has been no inbreeding *since F*, because there are no repeat ancestors. If your goal in computing COI is to estimate the probability of inheriting two copies of the same allele from an ancestor that appears on both sides of the pedigree, then it is critical that you include ancestors as far back as possible.

Have you completed this unit? Then mark this unit as completed.

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 August 14, 2015

 carol beuchat

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More COI: inbred ancestors & related parents

If you're trying to assess the probability of an animal inheriting two copies of the same allele from an ancestor (in fact, this is the definition of coefficient of inbreeding), then two key things must apply:

- 1) The ancestor must appear more than once in the pedigree, and at least once on the sire's side and once on the dam's side;
- 2) The ancestor must appear in the generations of the pedigree being used for the calculation of COI.

Both of these might seem obvious, but the second one is the cause of many, many erroneous calculations of inbreeding. In a 5 generation pedigree with no ancestors repeated, there will be no evidence at all of inbreeding that happened in the 7th generation. Most pedigreed (i.e., registered, closed stud book) dog breeds were originally founded with only a handful of dogs, and in a small population it doesn't take long before there are no more "non-related" animals to breed with and inbreeding increases relentlessly. So you should usually assume that a breed has significant inbreeding very early in the pedigree, and using shallow pedigrees (even 10 generations) can completely miss this old inbreeding.

What can you do about this? Use the entire pedigree database back to original founders. And if you doubt that this is necessary, the best way to prove yourself wrong is to start at the BEGINNING of the pedigree with the original founder dogs and do some COI calculations for some dogs in generations 8 or 10. The founders will by definition have no recorded parents (or their names would be in the database) and are assumed to be unrelated (which of course they probably are not), so their offspring will all have $COI = 0$. These animals provide the "baseline" against which we will assess inbreeding and loss of genetic diversity in the breed going forward. By reviewing what happened during the first 10 generations or so after founding, you will get a good idea of inbreeding and the strength of selection early in the history of the breed. Keep this in mind when you run COI for your current generation of animals. If COI in the breed was 16% at generation 10 after the breed was founded, your calculation of $COI = 7.8\%$ fifteen generations later is a fallacy.

You're going to work through several problems below, and the best thing to do is compute your answer for each then enter it in the quiz below, submit it, and see if you got it right. All the ones you haven't marked yet will get the red X but just ignore those. You'll fill in each of those one at a time as you work the problems. This way you'll know you're doing things correctly as you go, instead of working through all the problems, taking the quiz, and discovering that you're making a mistake at the top.

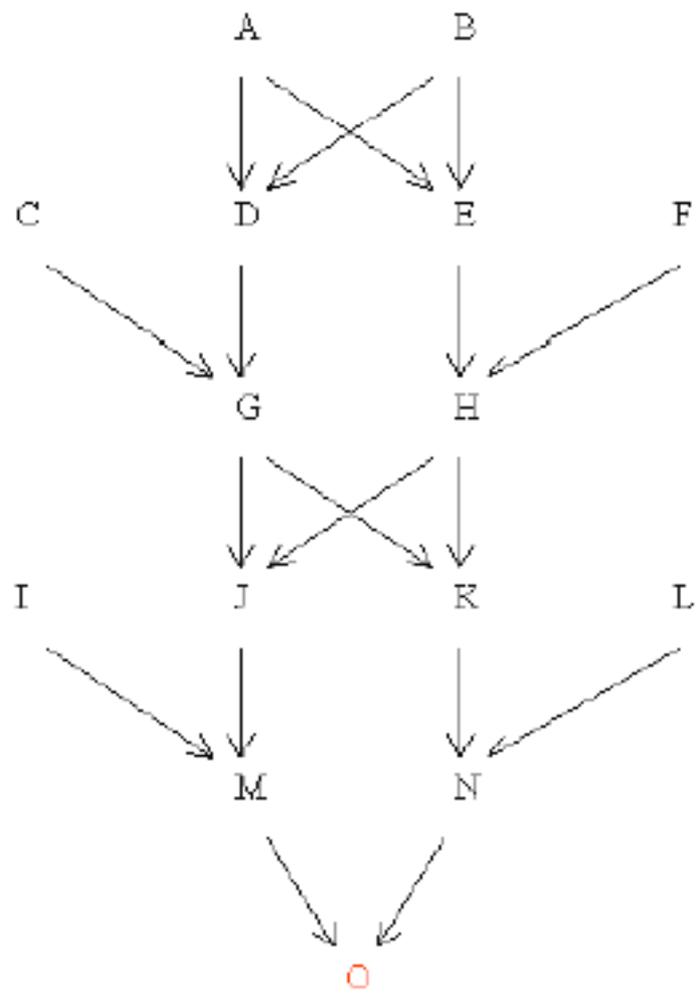
How do you account for inbred ancestors?

One thing you need to remember when there is early inbreeding is that inbreeding is additive. If you know an animal in your 10 generation pedigree is inbred, but the ancestors involved in that inbreeding are not in those 10 generations, it won't be accounted for when you calculate the 10 generation COI. But since inbreeding is additive, you can include that animal's inbreeding in your calculation if you know what it is; e.g., you computed that animal's inbreeding back to founders.

Question 1

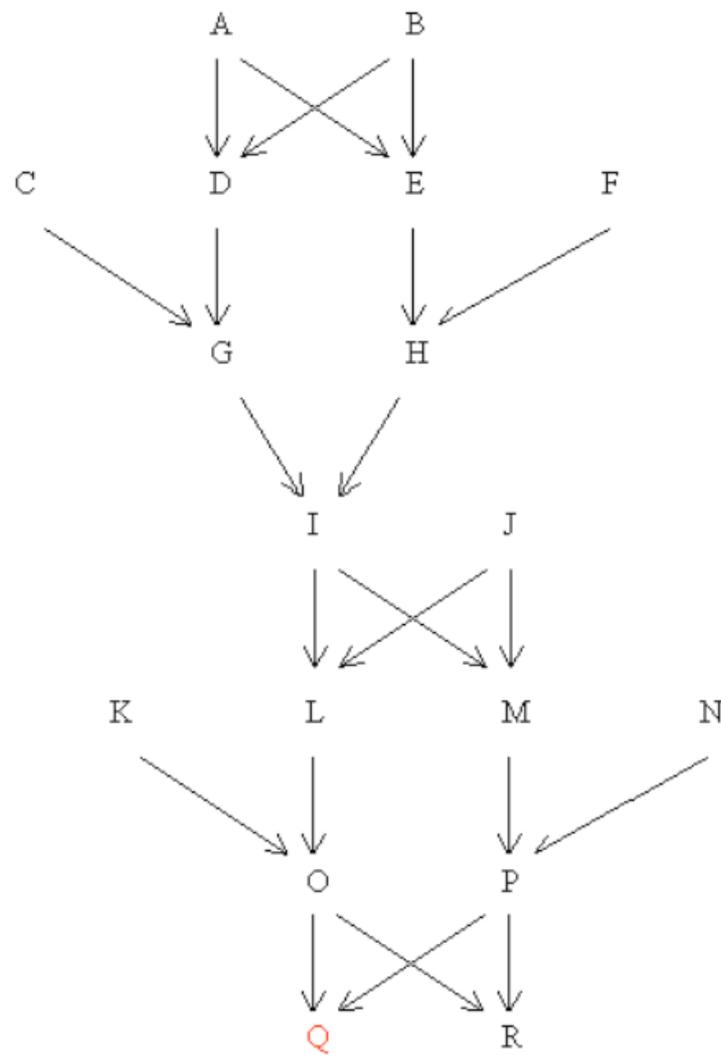
Let's look at an example. Calculate Wright's F (remember, F is the symbol for the coefficient of inbreeding) for animal "O" in this pedi-

gree. Use what you've learned about identifying the loops through the shared ancestors (there are 6 that you need to find).



Question 2

Next, look at this pedigree for animal "Q", whose parents have a common ancestor "I" who is inbred.



So first you need to compute the F for animal "I", then use this number when you calculate F for animal "Q". You know that there is a factor of 1/2 (0.5) with each animal when you work out the paths of the loop. If we write that as an equation, it will be

$$F_x = (0.5)^n$$

where x is the animal we're interested in, and the superscript (^) "n" is the number of animals that you counted in the path. This is how you have been computing COI so far. Now we will modify the equation to account for an inbred animal -

$$F_x = [(0.5)^n \times (1 + F_z)]$$

The first part of the equation is the same as the one above. To it we have now added the term for the inbred ancestor (which we'll call "Z"). This term is (1 + Fz), the correction for this inbred ancestor, where Fz is calculated just like you did for X by using the path method on the loops through the common ancestor. So figure out the COI of Q just like you have before, but calculate it for the ancestor "I", then for "Q" without including animals G, H and above, then plug those numbers into the equation where they go, which will be:

$$F_i = (0.5)^n \text{ (using the loops from I through the common ancestors A and B)}$$

and

$$F_q = (0.5)^5 \text{ (using the loops from Q through the common ancestors i and j)}$$

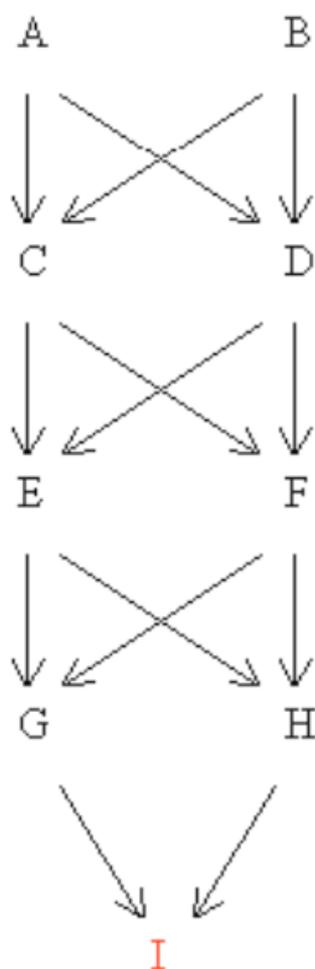
Then plug those numbers in this equation:

$$FQ = Fq \times (1 + Fi)$$

So the point here is that when you are using less than the complete pedigree database back to founders, earlier inbred ancestors DO matter in the calculation of total inbreeding.

Question 3

Let's do another one:



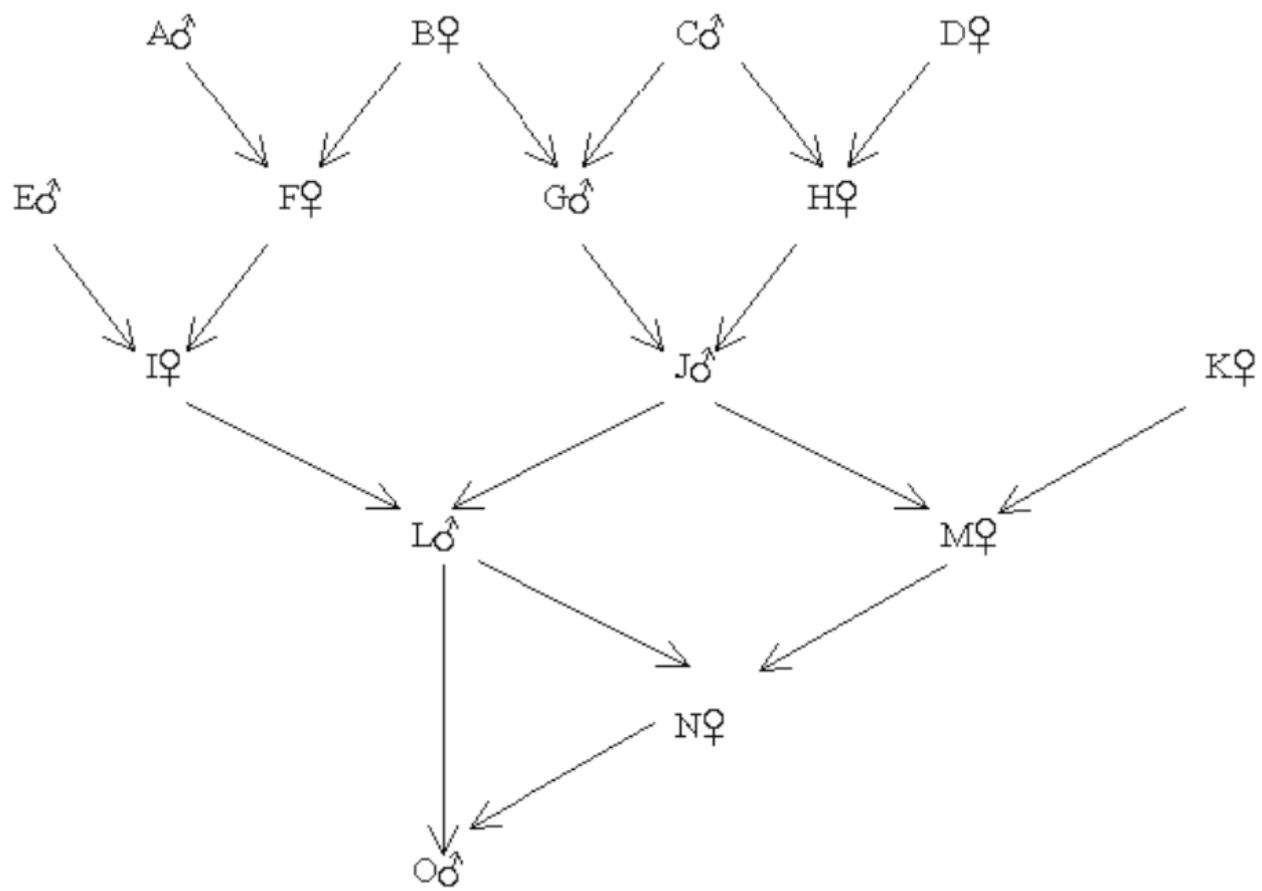
Here, you have multiple inbred ancestors. So go through the same steps you did above.

First, identify the animals that are inbred and figure out the loops. Calculate the inbreeding for each of those inbred animals separately like you did above. Then you include the inbreeding values for these ancestors as a term $(1 + F_x)$ for each that is multiplied in the equation as above. Don't let the math scare you. It's just like before, but with an extra step added for each inbred animal.

Remember, you need to trace all possible paths from I through each ancestor, and for ancestor A, for example, there will be 4 paths to trace. (Tip: starting from I, got to G, then from there you will see that you have two paths to follow through E and F, and likewise from each of those there are 2 paths.)

Question 4

Okay, just one more, and you'll be done doing COI calculations by hand forever! This one isn't as complicated as it looks. Start with the offspring O (at the bottom) and trace the 3 possible paths through common ancestors.



Make sure you did each problem correctly by submitting your quiz answers. When you get them all right, give yourself a treat - you've earned it!

Inbred ancestors & related parents

You'll need to correctly answer at least **3 of the 4** questions below (**at least 70%**) to progress to the next unit.

Question #1 - What is the COI of animal O in Question 1?

- > 1%
- > 5%
- > 7%
- > 12%
- > 21%

Question #2 - What is the COI of animal Q in Question 2?

- > 3.3%
- > 6.5%
- > 9.8%
- > 13.1%

> 21.5%

Question #3 - What is the COI of animal "i" in Question 3?

- > 3%
 - > 25%
 - > 33%
 - > 45%
 - > 50%
-

Question #4 - What is the COI of animal "O" in Question 4?

- > 7.9%
 - > 15.8%
 - > 26.2%
 - > 33.2%
 - > 49.9%
-

[« Previous Unit](#)

[Next Unit »](#)

🕒 August 14, 2015

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More COI: Inbred Ancestors & Related Parents (*answers*)

Answers to the quiz questions -

QUESTION #1

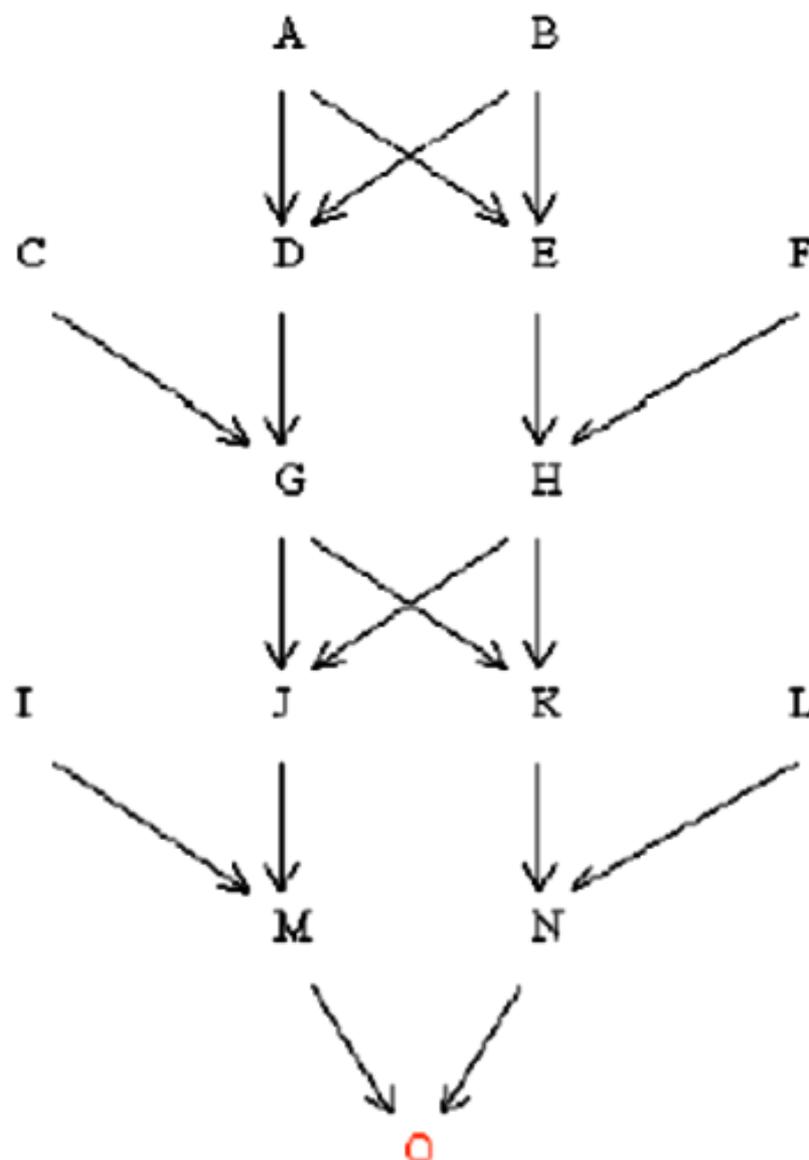
None of the common ancestors A, B, G or H are inbred. Therefore, no corrections for inbred ancestors are necessary.

G: M-J-G-K-N (5 steps) $(0.5)^5 \times 2$
 H: M-J-H-K-N (5 steps)

A: M-J-G-D-A-E-H-K-N (9 steps) $(0.5)^9 \times 2$
 A: M-J-H-E-A-D-G-K-N (9 steps)

B: M-J-G-D-B-E-H-K-N (9 steps) $(0.5)^9 \times 2$
 B: M-J-H-E-B-D-G-K-N (9 steps)

So, F for animal O = $(0.03125 \times 2) + (0.001953 \times 4)$
 $= 0.0703125$, or 7.03%



QUESTION #2

The parents of animal Q have an inbred common ancestor (i). So we need to compute the F for animal I separately -

A: G-D-A-E-H (5 steps) $(0.5)^5$

B: G-D-B-E-H (5 steps) $(0.5)^5$

So $F_i = 0.0625$, or 6.25%

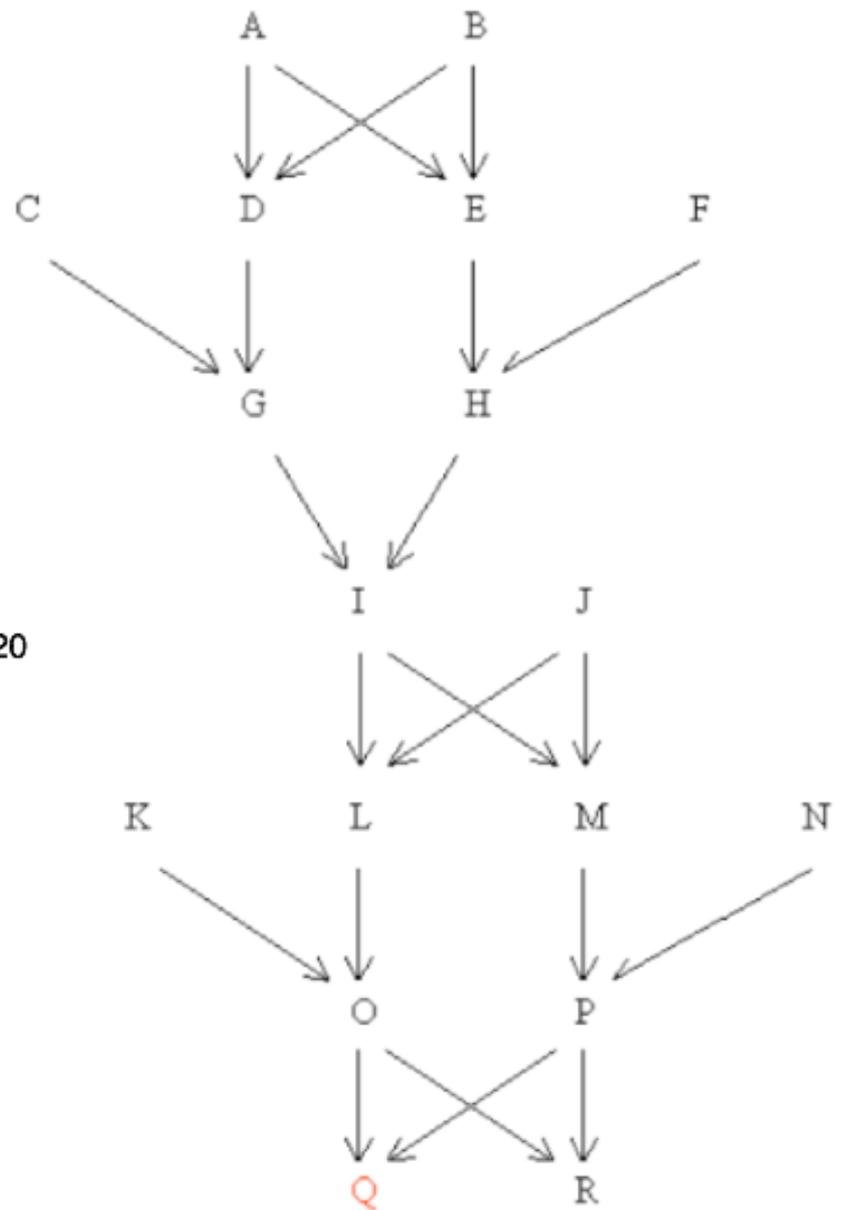
And for the lower part:

I: O-L-I-M-P (5 steps) = $[(0.05)^5] \times (1 + 0.0625) = 0.03220$

J: O-L-J-M-P (5 steps) = $[(0.05)^5] \times (1 + 0) = 0.03125$

** Remember that the equation for the lower part of the pedigree must include the term for the inbred ancestor i : $(1 + F_i)$

So $F_q = 0.03220 + 0.03125 = 0.06445$, or 6.45%



Question #3

This is 3 generations of full-sib matings, so the common ancestors of G & H are A, B, C, D, E, & F.

E and F are inbred (through related parents).

a) Calculate F_e and F_f

A: C-A-D (3 steps); $(0.5)^3 = 0.125$
 B: C-B-D (3 steps); $(0.5)^3 = 0.125$

so $0.125 \times 2 = 0.25$ (or 25%)

b) Calculate F_i

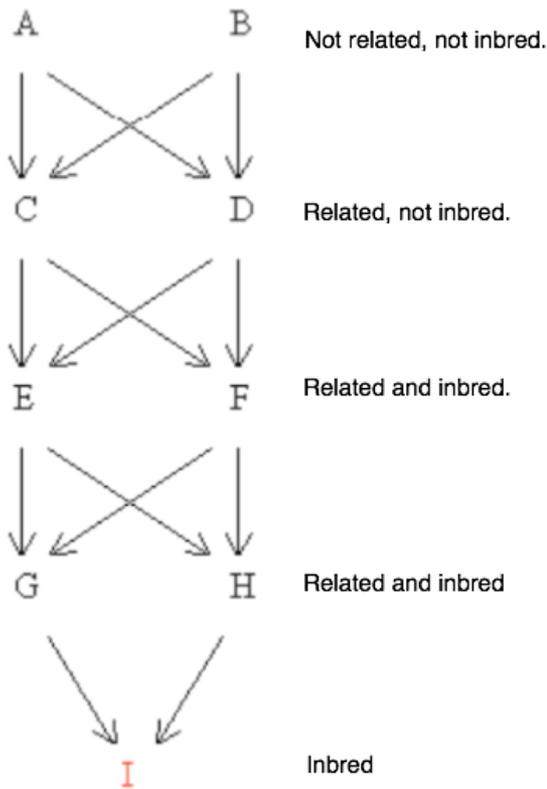
** remember to include the term for the inbred ancestor -- $F_i = [(0.5)^n] \times (1 + F_a)$

E: G-E-H (3 steps); $(0.125) \times 1.25 = 0.15625$
 F: G-F-H (3 steps); $(0.125) \times 1.25 = 0.15625$

C: G-E-C-F-H (5 steps)
 C: G-F-C-E-H (5 steps)

D: G-E-D-F-H (5 steps)
 D: G-F-D-E-H (5 steps)

** for the C and D paths, each = 0.03125



- A: G-E-C-A-D-F-H
- A: G-F-C-A-D-E-H
- A: G-E-D-A-C-F-H
- A: G-F-D-A-C-E-H
- B: G-E-C-B-D-F-H
- B: G-F-C-B-D-E-H
- B: G-E-D-B-C-F-H
- B: G-F-D-B-C-E-H

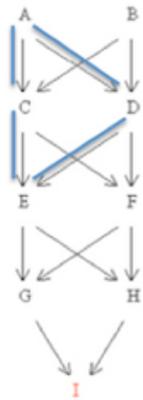
All of the A and B paths have 7 steps; so $(0.05)^7 = 0.0625$

SO:

$$0.15625 \times 2 + 0.03125 \times 4 + 0.06250 \times 8$$

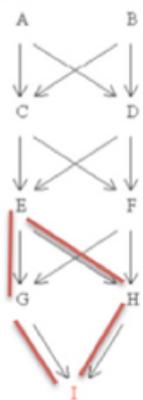
0.5000

or, $F_i = 50\%$



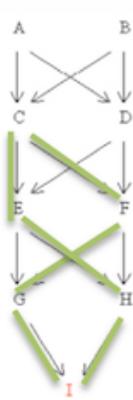
A & B

3 x 2



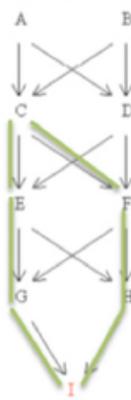
E & F

3 x 2



C & D

5 x 2



C & D

5 x 2



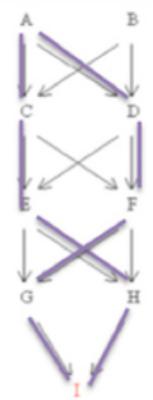
A & B

7 x 2



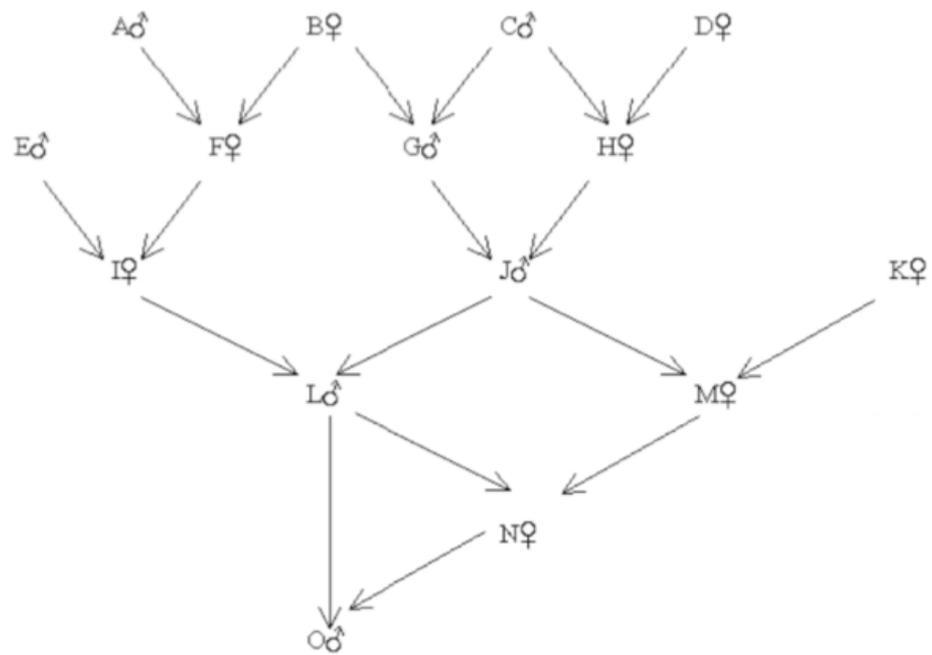
A & B

7 x 2



A & B

7 x 2



Take care of the easy ones first:

$F_i = 0.125$
 $FL = 0.03125$

Then:

<u>Common ancestors (of parents L and N)</u>	<u>Paths</u>	$(1/2)^{n+1}$	$(1 + F_A)^*$	
None	L - N	$(1/2)^2$	x 1.03125	= 0.2578125
J	L - J - M - N	$(1/2)^4$	x 1.125	= 0.0703125
B	L - I - F - B - G - J - M - N	$(1/2)^8$	x 1.0	= <u>0.00390625</u>
				<u>0.33203125</u>
				<u>$F_o = 33.2\%$</u>

Now, invest in a copy of some good pedigree software and you'll never have to calculate your own COIs again!

Have you completed this unit? Then mark this unit as completed.

Mark as Completed

« Previous Unit

Next Unit »

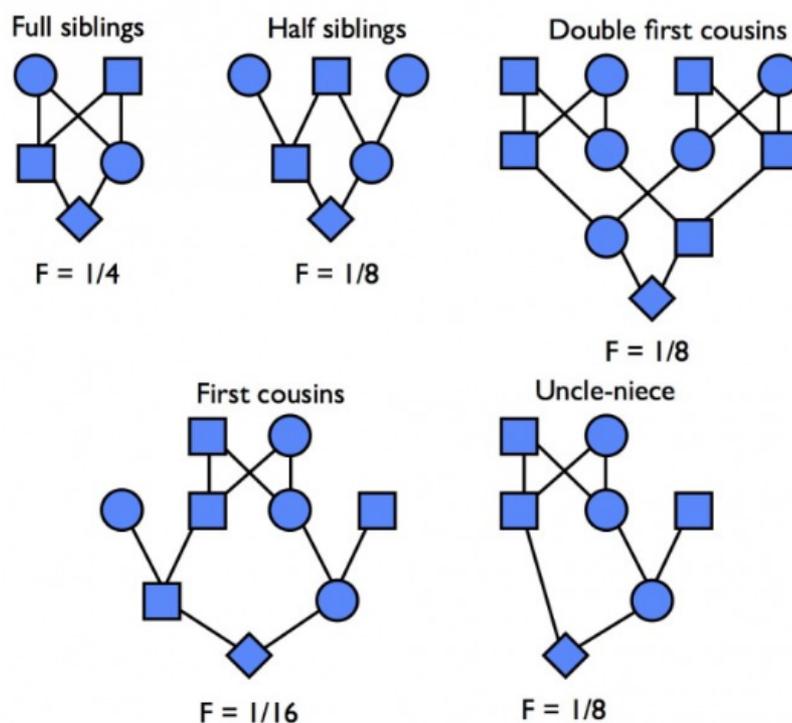
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How many generations of pedigree data do you need? (pt 1)

Now that you understand how COI is calculated, you should be able to apply what you know to this question.

You know that the position of a common ancestor in a pedigree (common on both the dam and sire's side of the pedigree) affects COI of an animal - for every generation the common ancestor is deeper in the pedigree, the probability of inheriting two copies of the same allele from that ancestor goes down by half. BUT, if that ancestor occurs more than once, ALL of those must be included in the calculation of the pedigree.

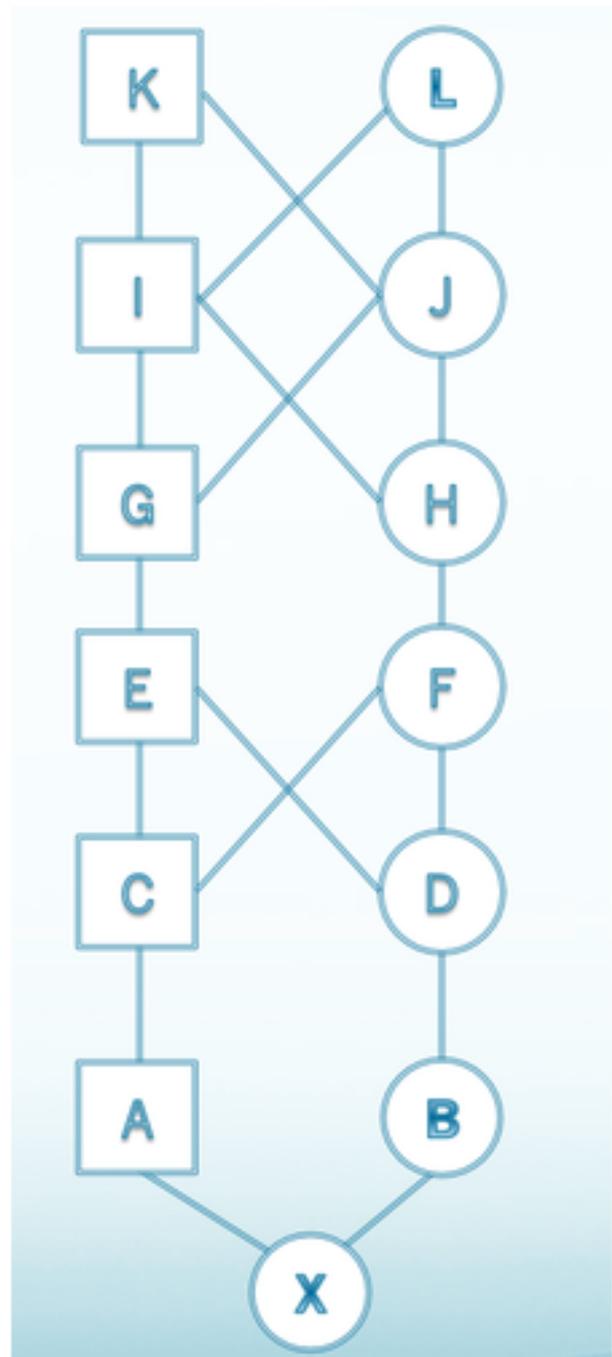
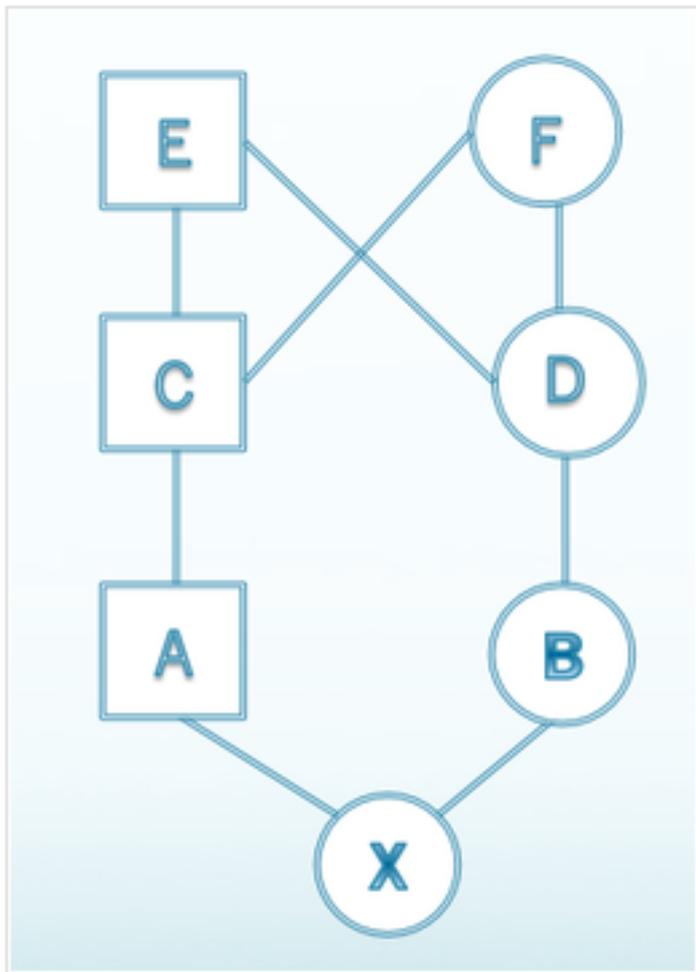
You saw in one of the quiz questions (#3 of Pedigree Structure) how you could have three very different (but cleverly arranged) pedigrees - with a common ancestor appearing at various positions and multiple times in a pedigree - and get exactly the same COI for the dog of interest. And that same concept is illustrated here, where several different pedigrees can result in the same COI (in this case 1/8, for half-sibs, double first cousins, and uncle-niece).



Sample Inbreeding Calculations. Adapted from 'Principles of Genetics'

You will recognize the pedigree of dog X below (left) from the video tutorial on calculating COI. We computed the COI of animal X to be 6.25% based on this pedigree.

Let's say that digging around in the attic, you found some old kennel records and were able to add some information to this lineage of dogs, and the new, improved pedigree for X is below (right). If you do the calculations for the COI of X based on the new pedigree, you're going to get a different value than you did for the old pedigree.



Now, if you're using calculations of COI to inform your breeding decisions, for example to give you information about potential homozygosity of animal X (to assess prepotency and/or risk of a disease caused by a recessive mutation), then the value you get from the first pedigree will not be correct because it does not include the information about ancestry several generations back that will affect the value of COI (i.e., the sib-sib mating of I and J). The COI of the first pedigree only reflects the inbreeding that occurs during the generations displayed. The COI calculated from the second pedigree includes additional information that will affect the predicted level of inbreeding. Which of these is correct?

If (for some reason) you are only interested in recent inbreeding, then you would use only the pedigree data for the period you're interested in. If however, you want a true assessment of potential homozygosity, then you should use ALL of the pedigree data for that animal, as far back as you have information for. Most closed populations of purebred dog breeds (i.e., the stud book is closed) all descend from only a few individuals, and if the pedigree database doesn't go back far enough to include the early inbreeding, it won't be included in calculation of COI.

In practice, there are a few things to consider that might let you get away with using fewer generations.

* If you calculate the COI of a potential mating using 8 generations of pedigree data and the value you get is 42%, that might be all

you need to know. Since COI will only increase as you include more information, if 42% is already unacceptably high, then that's all you need to know.

* Let's say you have a break in the pedigree data 10 generations back, and you're unable to establish the actual relationships before and after the break. You know that the calculation of COI assumes the animals in the oldest generation of the data are unrelated (i.e., have a COI of 0%). When there is a break in the data, you KNOW the last generation of animals before the break must be related if they're more than a few generations from the founders. So you could calculate the COI from founders to the beginning of the break, and use that information to adjust the COI of the first generation after the break, in the same way that you accounted for inbred ancestors in the quiz questions for inbred ancestors and relatives (unit 5 of this module).

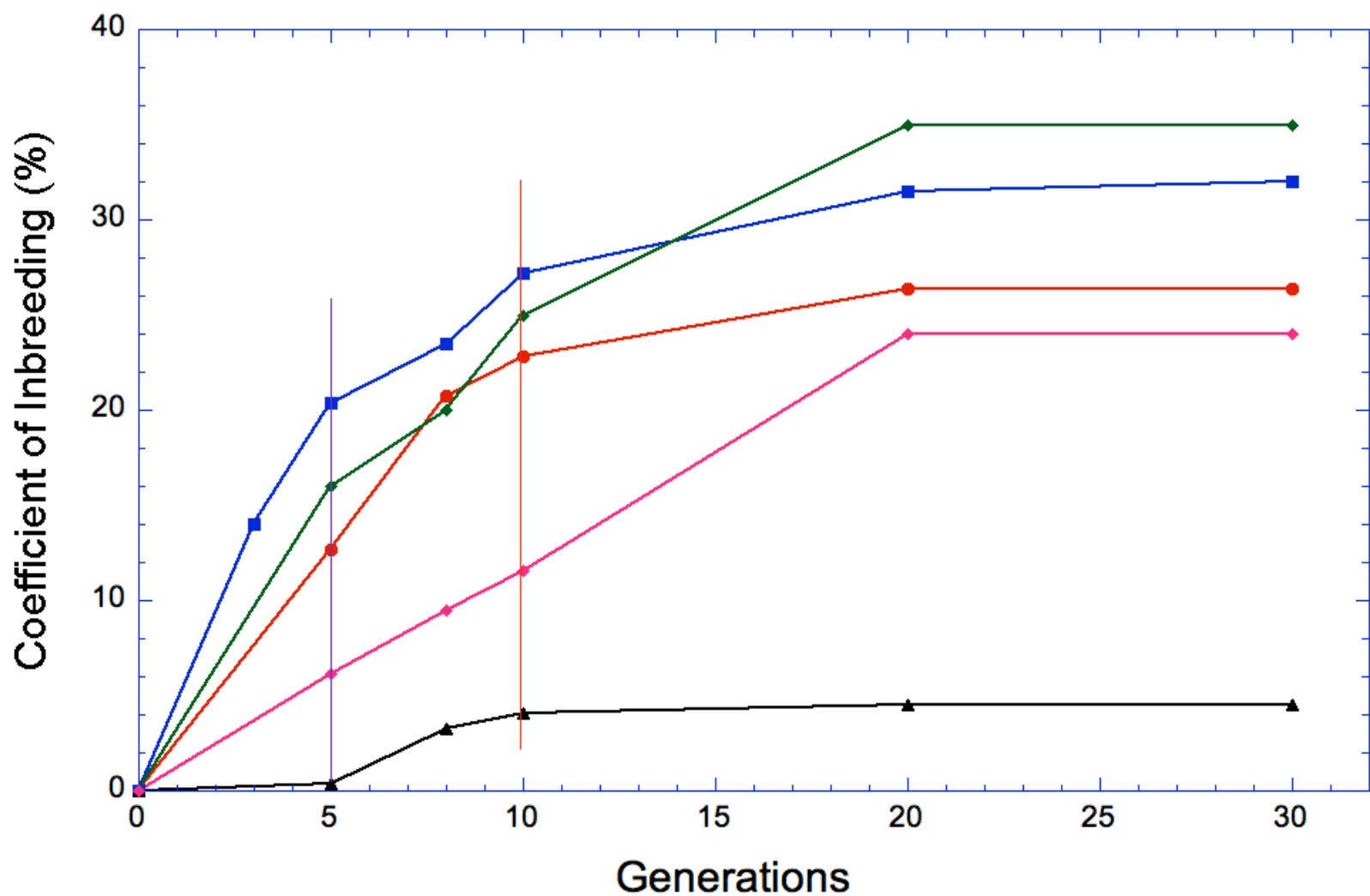
* Many breeds went through severe bottlenecks in their history. Many breeds were nearly wiped out during the World Wars (especially WWII), there were distemper epidemics, popularities of breeds rose and fell, etc. If the breed was reduced at some point to only a handful of dogs, you usually won't be making a big mistake to compute COI since that bottleneck. And as above, if you have some idea of how related the dogs were that survived the bottleneck, you can adjust the calculation of COI for the approximate level of inbreeding in those dogs instead of assuming they are completely unrelated.

How Does COI Change with the Number of Generations?

It seems like everybody has an opinion about this. Some use 5 generations, some 8, and some 10. Relatively few people use more generations than this, perhaps because often pedigree software won't do more than this, or if it does it gets very slow.

So let's look at some data. These are some numbers I computed from pedigrees of several different dogs. One had very low inbreeding (< 5%), the others had significantly more. For each of these individuals, though, the way the computed COI changed with the number of generations of data used was different. One thing is clear - unless the level of inbreeding is very low, or the pedigree very shallow, using only 5 generations of pedigree data is likely to be extremely misleading. In this figure, it's easy to see how far wrong you can go. One animal (pink) has a COI at 5 generations of about 6% (not bad); at 10 generations it is up to about 10% (still not so bad); but including 30 generations of data reveals that the true COI is about equal to what you would get from the mating of full siblings (25%). If you're worried about the probability of producing puppies with a genetic disorder caused by a recessive mutation, there is a whopping difference between the relatively low risk of about 1 in about 20 (6% with 5 generations) and 1 in 4 (25% using 30 generations).

Does it matter how many generations you use when calculating COI? How many generations should you use? As many as you can.



Playing with Pedigrees

It's worth playing around with actual pedigrees to get a feel for some of these concepts. Let's have a look at some data for a whippet.

Go to the "[Whippet Archives](#)", a nice example of a pedigree database. (If for some reason you don't have access to this website, I've created a page with the things I want you to see [HERE](#).) From the menu bar at the top, select "Dogs" then "Search Dogs". For "Year of Brith" select "201x" then "Search". That will bring up the youngest dogs in the database. Select "Jaytea Alive and Kicking", who was born in 2011 (and usually comes up first on the list).

Go to her page, which has her information (breeder, titles, health tests, etc) and her pedigree at the bottom. The default for the pedigree is 3 generations, and you'll see in the oldest generation that "Chelsea Gold Rush of Keynote" appears on both the sire's and dam's sides of the pedigree. Just above the pedigree on the right you can select "Pedigree Analysis" - do that.

Now we have a page of statistics. At the top you will see her coefficient of inbreeding (10.93%), which has been calculated using 7 generations of data, so it includes the dog that appears twice in the third generation. Now at the top of the page, change the number of generations in the calculation to 2 - you will see the calculated COI go to 0.00%. Change the number of number of generations stepwise from there all the way to 10, and the COI will go higher with each generation, to 15.57% for 10 generations, which is the maximum number of generations offered. You might have noticed the delay in the last calculation - it will take longer to compute each additional generation because the number of animals in the pedigree is increasing with each generation. Sometimes the change in COI with each additional generation used in the calculation starts to level off by about 10 generations, but sometimes it doesn't. This will depend on the history of the breed - number of founders, how long the breed has been around (which affects the number of generations), whether there were bottlenecks, and so on.

Pedigree Analysis for Jaytea Alive And Kicking

Coefficient of Inbreeding (COI): ?

Jaytea Alive And Kicking: **7.81% (5 generations)**

Analysis Summary ?	# of dogs	Gen1	Gen2	Gen3	Gen4	Gen5
Actual ancestors in 5 generations	46	2	4	7	13	24
Maximum ancestor count	62	2	4	8	16	32
Ancestor loss	16					
Ancestor loss %	25.8%					

Ancestor	Sex	Blood% ?	Partial COI (COI Contribution) ?	# of appearances	Gen1	Gen2	Gen3	Gen4	Gen5
Shannon Down French Kiss	♀	50.00%	0.00%	1	1				
Snow Hill Indecent Proposal	♂	50.00%	0.00%	1	1				
Bohem Circus Runaway	♂	31.25%	3.12%	2		1		1	
Chelsea Gold Rush of Keynote	♂	28.12%	3.12%	3			2		1
SDW Diamondtheruff V Hasue	♀	25.00%	0.00%	1		1			
Summit N Snow Hill Shared Gold	♀	25.00%	0.00%	1		1			
Chelsea Long Kiss Goodnight	♂	25.00%	0.00%	1		1			
Bohem All About Eve	♀	15.62%	0.00%	2			1		1
Rhode Paved With Gold	♂	15.62%	0.39%	3				2	1
Jocora Chelsea One For The Road	♀	12.50%	0.00%	2				2	
Chelsea Calibri	♀	12.50%	0.00%	1			1		
Phantom Diamond N Lace V Hasue	♀	12.50%	0.00%	1			1		
Summit Heavenly	♀	12.50%	0.00%	1			1		
Starling's Bojan On	♂	12.50%	0.78%	2				2	

There is some additional information offered here that is useful. There is a table that shows "ancestor loss" for each generation, computed from the total number of dogs in the pedigree vs the number of unique dogs in the pedigree (so a dog might appear 3 times but is only counted once). In a pedigree with lots of inbreeding, there are many fewer unique ancestors.

Below this are data for % Blood, which is a way of evaluating the contribution of an individual dog to the genetics of the focal dog. It uses information about how each dog is related to the others as well as how far back in the pedigree and how many times it appears.

Just to the right of the COI table at the top, you'll see "What do all these numbers mean". Select that and you'll get a page that provides a very useful summary of the information provided by this website and how the values are calculated.

So what is the TRUE inbreeding coefficient of our whippet - Jaytea Alive and Kicking? We don't actually know because this site doesn't do the calculation including ALL ancestors back to founders. We know it's at least 15%, and we know that is almost certainly an underestimate. Perhaps the true value computed back to founders is 18%, but it could be 30%. It would depend on pedigree history that we have no information about unless we follow the pedigree of this dog back to founders and compute it ourselves.

Repeat what we've just done here with a few other dogs in the whippet database. You will find some dogs with very low inbreeding at 10 generations, and others that are very high. And you should realize how easily COI can be misused by somebody who doesn't understand how the calculations are performed and what they are intended to tell you. As we discussed earlier, COI computed on 5 generations of data can only tell you about inbreeding in those five generations. It tells you nothing about "how inbred" a dog is because it doesn't include very much of the dog's history.

There are online pedigree databases for many breeds, some modeled after this one and others of different design. Some also present a coefficient of inbreeding for each dog, but if it doesn't stipulate how many generations were used in the calculation, it's meaningless.

One other **BIG** caveat - if one or both parents of a dog are missing in a pedigree, all the ancestors of that dog are removed from these calculations and that dog's COI is considered to be 0%. Whoever is bred to that dog will produce puppies with COI = ZERO, because the dam and sire have no shared ancestors (because one dog's history is completely missing). This is a HUGE problem with on-line databases. Without tracing a pedigree back looking for missing dogs, you have no idea if the COI has any meaning.

Also, the data in many of these databases are entered by breeders, and if a dog's name is spelled one way in one place and a bit differently somewhere else, the computer assumes they are different dogs, which will also separate a dog from its relatives. A dog named "The Colour Purple" in one place and "The Color Purple" someplace else in the pedigree database is going to cause problems. "MyKennel's Rascal" and "MyKennels Rascal" and "My Kennels Rascal" are all different dogs to the computer. Checking for database errors is absolutely essential if the data are going to be correct.

How many generations do you need?

You'll need to correctly answer at least **3 of the 4** questions below (**at least 70%**) to progress to the next unit.

Question #1 - Ten generations of pedigree data are usually enough to produce an accurate estimate of COI.

- > True
 - > False
-

Question #2 - You can use COI to get information about both recent and old inbreeding in the pedigree of a dog.

- > True
 - > False
-

Question #3 - Missing data in a pedigree database will cause your estimate of COI to be

- > an overestimate
 - > an underestimate
 - > doesn't really matter
-

Question #4 - As you add additional generations to the pedigree database of an animal, the estimate of COI might actually go down.

- > True
 - > False
-

[« Previous Unit](#)

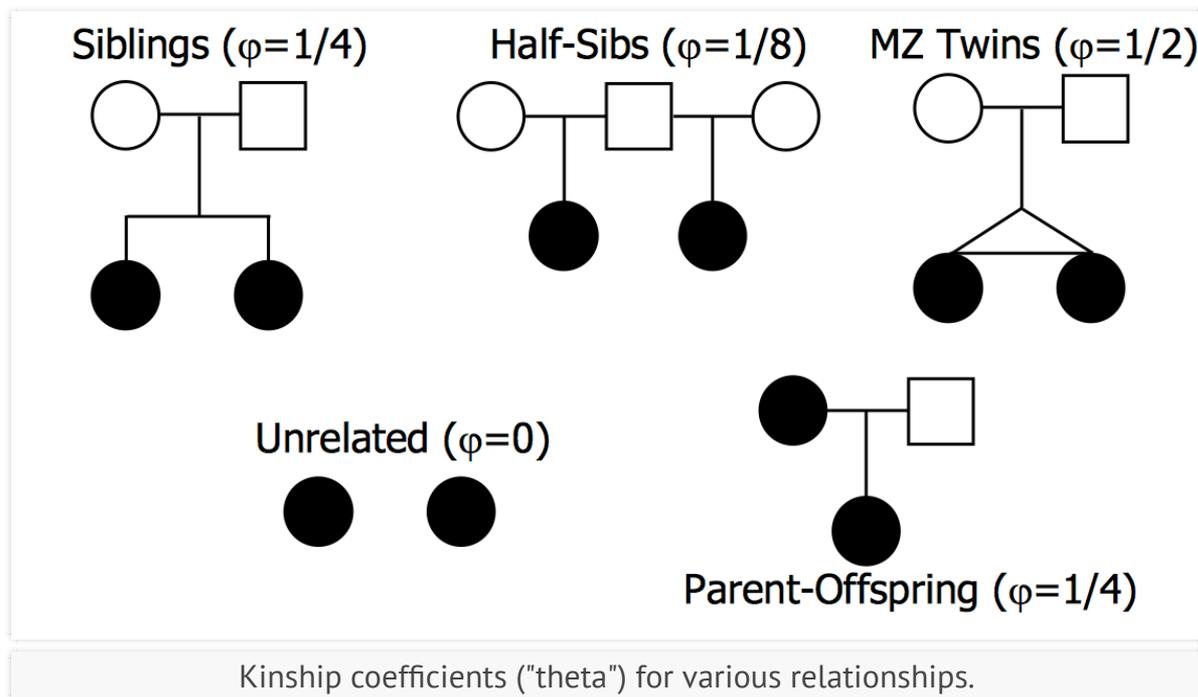
[Next Unit »](#)

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Inbreeding & Kinship (part 1)

In the broadest sense, two animals that share an ancestor are considered to be related. The common ancestor can be recent or many generations before the present, there are many possible types of relationship (e.g., half sib, uncle, great-grandfather), and the ancestor can appear not just once but multiple times in the pedigree. Genetic relationships can be complex and difficult to sort out just by looking at a pile of pedigrees. However, there are good tools available that can help you understand the relationships among individuals in a population as well as the structure of the population as a whole.

You have already learned about the coefficient of inbreeding, which expresses the probability of a particular animal inheriting two copies of the same allele from a common ancestor. A related and powerful relationship statistic is called "kinship" (also referred to as "coancestry"). Kinship is similar but refers instead to a pair of animals: specifically, it is the probability that two alleles sampled at random from the same locus of two individuals are identical by descent. Note that kinship is a *comparison of the genetic similarity between two animals*. Two animals that share many ancestors will share more alleles that are identical by descent, so their genomes will be similar to each other simply as a consequence of their shared ancestry.



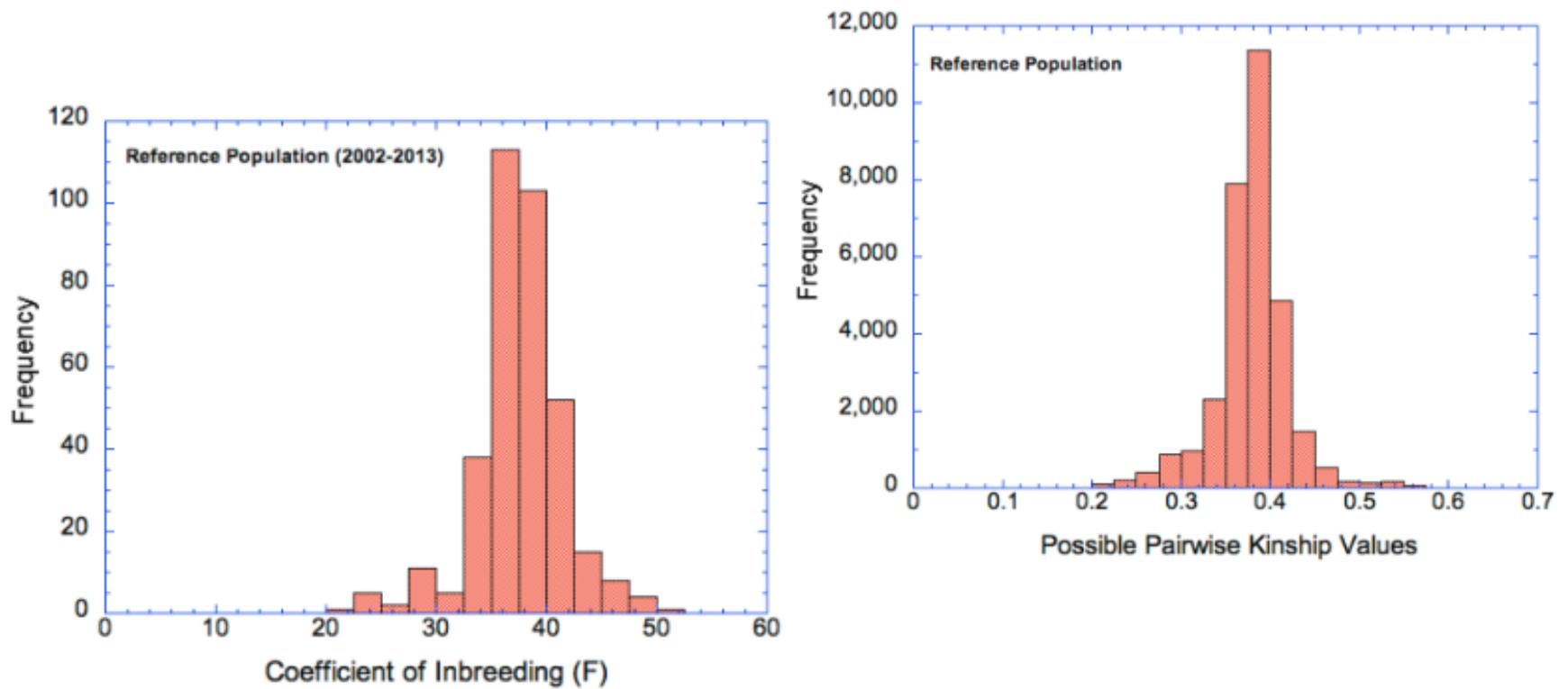
The similarities in the definitions of coefficient of inbreeding and kinship are not accidental - *the coefficient of inbreeding of an animal is equal to the kinship coefficient of its parents*. So a pair of animals with a high kinship coefficient are genetically more similar than another pair with a low kinship coefficient. Like COI, kinship coefficients run from 0 to 1 (0 to 100%).

What does the kinship coefficient tell us?

If kinship is so similar to COI, why do we need it? The coefficient of inbreeding is a number that is specific to a particular individual. Kinship, on the other hand, specifically refers to genetic relationship or similarity between two individuals, or between one animal

and a group of animals. So for example, if you had a table of the kinship values for every possible male-female pair in a population of animals, the pairs with the highest values would be most closely related (and therefore likely to be genetically most similar) and the pairs with the lowest would be least related. If you wanted to reduce the risk of genetic diseases caused by recessive mutations in a litter of puppies, you would choose among the potential mates with the low kinship coefficients. In actuality, this is the same information you would get if you did all possible pairwise test matings and determining the coefficient of inbreeding of the puppies that would result. But kinship can also be used to reveal important information about the genetic structure of a population and the "genetic value" of particular individuals to the breed as a whole.

Let's say you generated a table of all possible pairwise kinships of the current reproductive population of your breed and that you also had the COI for all of these animals. You could then examine the frequency histograms of these two sets of data:

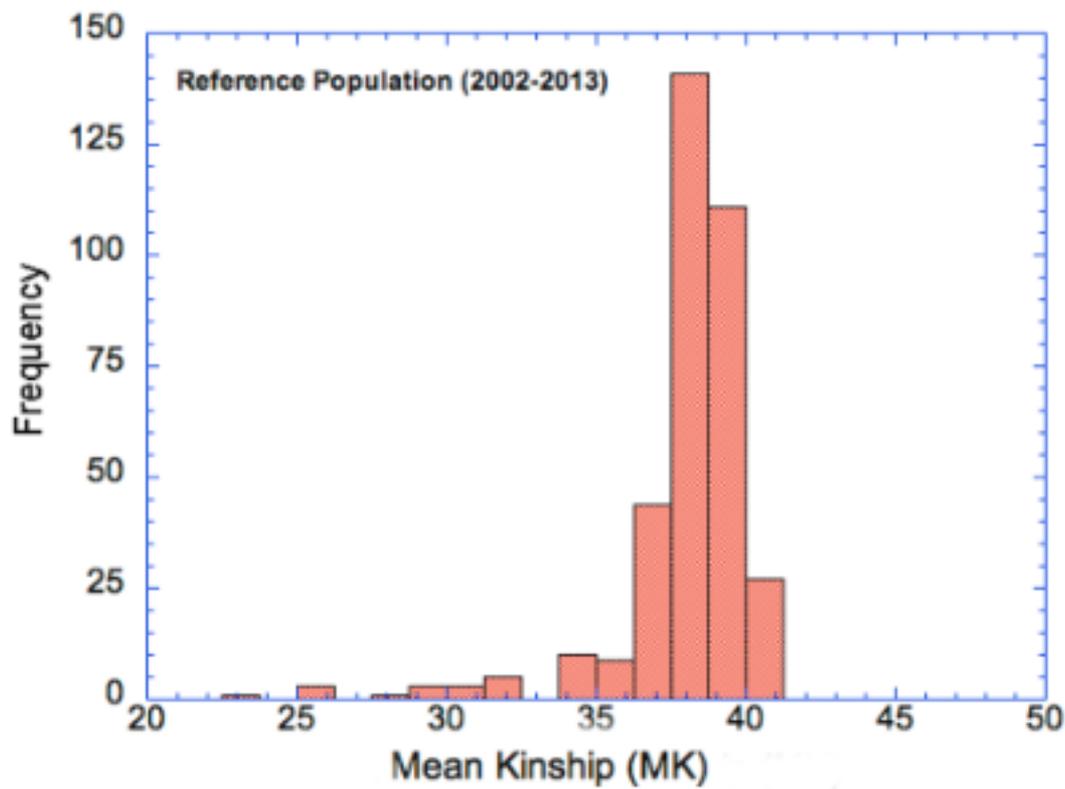


* Note the difference in the axes - the coefficient of inbreeding data are as percent (0-60%) and the kinship data as a fraction of 1 (0-0.7), so 40% on the COI graph is the same as 0.4 on the kinship graph.

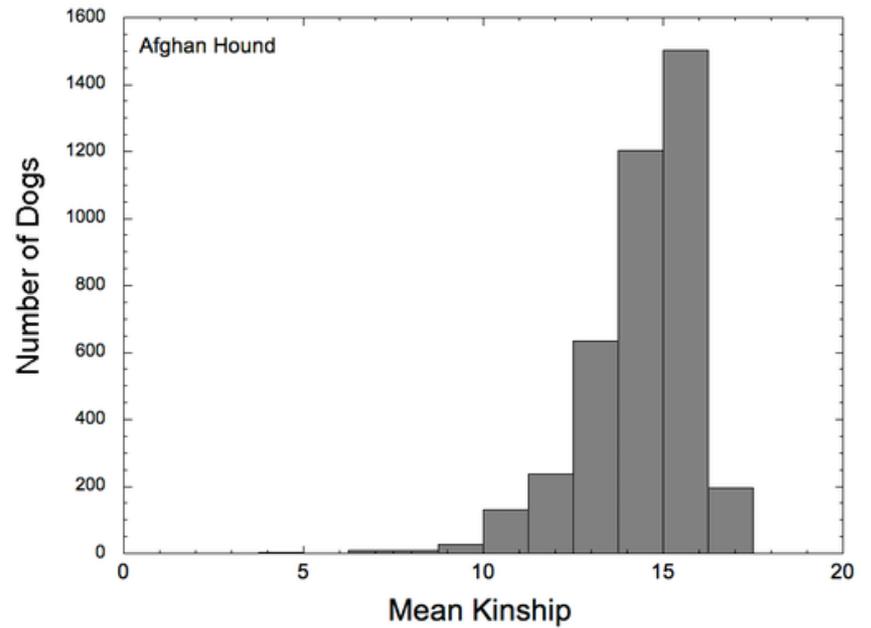
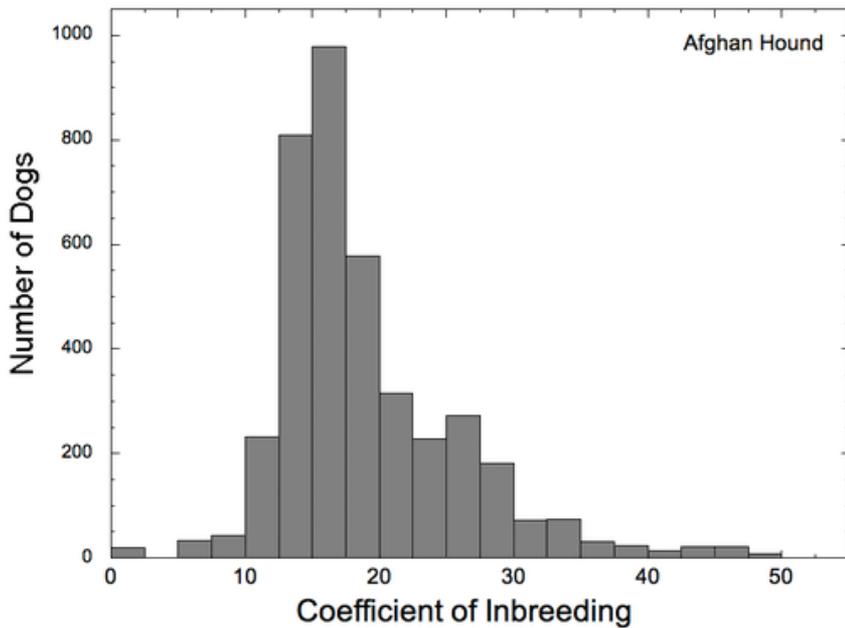
For this breed, the COI graph (left) indicates that the most of the population has COI greater than about 35%, with some as high as 50%. The graph of pairwise kinship values (on the right) is very similar, but notice that the numbers on the y-axis are much higher because the COI graph depicts the actual coefficients of individuals in the population, whereas the histogram of kinship values depicts all possible pairwise combinations (including with itself).

If these graphs were different, that would indicate that there was a bias towards producing animals with higher (or lower) COI than their statistical representation in the population. If breeders were to preferentially select breeding pairs that fell in the left tail of the kinship graph, the result would be lower COI in the offspring and a shift in both graphs to the left. (This would be a good thing.) The fact that there is a lower tail on the kinship graph means that it is possible for breeders to reduce the overall level of inbreeding in the population (at least a bit) by choosing pairs with lower kinship.

Now look at this third graph. Let's say we have animal A in a population of animals. We can compute all the pairwise combinations of kinship between A and animals of the opposite gender - e.g., A to B, A to C, A to D, etc (like we did above). The average of all of those kinships involving A and another individual is the mean kinship for animal A. We could then do the same for animal B, and for C, etc and have a list of "mean kinship" values for the animals in the population.



Let's look at another example. Note first that the scales on these two graphs are different (0-60% for COI, 0-20% for kinship). In this case, you can see that there are many dogs in the population with COI > 20% (and a few greater than 40%!), even though the distribution of mean kinship peaks at about 15% and drops off steeply after that. This indicates that breeders are deliberately choosing to very closely inbreed, producing offspring that are far more genetically similar than full siblings (which would have COI of 25%).



Identifying "genetically valuable" animals

If you think about it, you will see that animals with lots of close relatives in the population will have a higher "mean kinship" than animals with very few relatives. There will be many more copies of the genes of the former than the latter, because all of these animals will be genetically similar. On the other hand, an animal with a low mean kinship will be genetically less similar to most of the population. From the perspective of genetic "resources" (or genetic diversity), animals with low mean kinship are *genetically more valuable* because their genes are relatively rare in the population. Losing a few of the individuals with high mean kinship won't affect the overall genetic composition of the breed much; losing a few animals with low kinship risks losing genes that are rela-

tively rare.

So, in the first set of graphs above, the one for Mean Kinship has high frequencies in the 35-40 range, but there are also some in a rather long tail to the left. These data are for a breed that did an outcross to another breed, and the descendants of that outcross stand out as having much lower average kinship than the animals in the main population. Relative to the population as a whole, those animals carry the greatest proportion of unique alleles, and by the definition we used earlier these animals would be considered to be "genetically most valuable". If preserving those rare alleles was a priority, then these animals would indeed be most valuable. In practice, there would probably be other considerations (e.g., aspects of type), but these could be weighed together with the genetic information.

Have you completed this unit? Then mark this unit as completed.

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[« Previous Unit](#)

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 August 14, 2015

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Inbreeding & Kinship (part 2)

Coefficient of inbreeding never changes; mean kinship does

There is a critical difference between COI and kinship coefficient that you need to understand. The COI of an animal is determined by who its parents are; that is, the COI of the animal is the kinship coefficient of its parents. COI is the same for all the individuals that share the same two parents (even in different litters). Likewise, the kinship coefficient of a pair of animals is determined by their relationship to each other, and that does not change.

On the other hand, an animal's mean kinship, and thus its genetic value to a population, is not a fixed value. Because mean kinship is calculated against all individuals in the population, addition or removal of animals will likely change the MK for everybody. For instance, a genetically valuable male (with a low MK) wins a big show and is suddenly a popular sire. Every puppy the new star produces reduces his own genetic value to the breed, because the frequency of his genes in the population increases (where genetic value goes down as the genes of an animal become more common in the population). So using MK as a way to identify genetically valuable animals requires that the all of the pairwise kinships for each animal be recomputed on a regular basis. We'll talk about an example of this below.

Using kinship to identify genetic "clusters"

We know that you can use kinship to determine the genetic similarity among animals, and that this allows you to evaluate the genetic value of individuals. You can also use kinship to do things like manage gene frequencies in a population, to prevent the loss of valuable subpopulations or rare alleles, and to monitor the genetic impact a popular sire is having on gene pool. We can do this using a mathematical technique called "cluster analysis".

Most populations of animal, and that includes purebred dogs, have what is called "genetic structure". By this we mean that there are identifiable subpopulations of animals that are genetically more related to each other than to animals in other subpopulations. You can imagine a huge family reunion, which includes everything from your parents and siblings to your 4th cousin twice-removed. You could gather people together in clusters based on their genetic relatedness to each other as well as their genetic distance from the core of the family. This has been done for the entire global population of pedigreed Icelandic Sheepdogs by Dr Pieter Oliehoek from the Netherlands.

The Icelandic Sheepdog is originally a landrace of dogs used for herding sheep in Iceland that are probably descended from animals brought to the island from Northern Europe hundreds of years ago. The dogs are adapted to the climate and landscape of Iceland, and have only in the last few decades come under the influence of kennel clubs and breeders with less interest in a working sheepdog. The registered "purebred" Icelandic Sheepdog breed was founded using 36 animals collected from remote areas of Iceland. Breeding within a closed studbook, genetic diversity of the breed declined over time, and eventually breeders became concerned about the health of the breed's gene pool.

A genetic analysis of the breed conducted by Dr Pieter Oliehoek (Netherlands) verified that there was reason for concern. From the original 36 founder animals (assumed to be unrelated), the population had grown to more than 2500 animals. However, over the generations the genetic diversity of the breed was reduced to what you would expect to find in a population founded with only 2.2

founders with no loss of alleles in descendants. The reason for this are discussed [elsewhere](#), but we want to look at what breeders were able to learn from cluster analysis of the breed's kinship data.

The graph below is called a "dendrogram" because it looks like the branching structure of a tree. Each of the colored bars is a cluster of genetically similar animals (based on kinship), and the size of the bar reflects the number of animals in the cluster except for the green group, which is 10 times the size depicted. You don't need to understand the details of the graph, just the fact that there were 8 genetically-identifiable groups of animals in the purebred population. Remember, the entire breed was the genetic equivalent of just over 2 animals, so analysis of kinship was able to reveal some fairly subtle variation within the population. This organized variation within a single breed reflects the "genetic structure" we mentioned earlier.

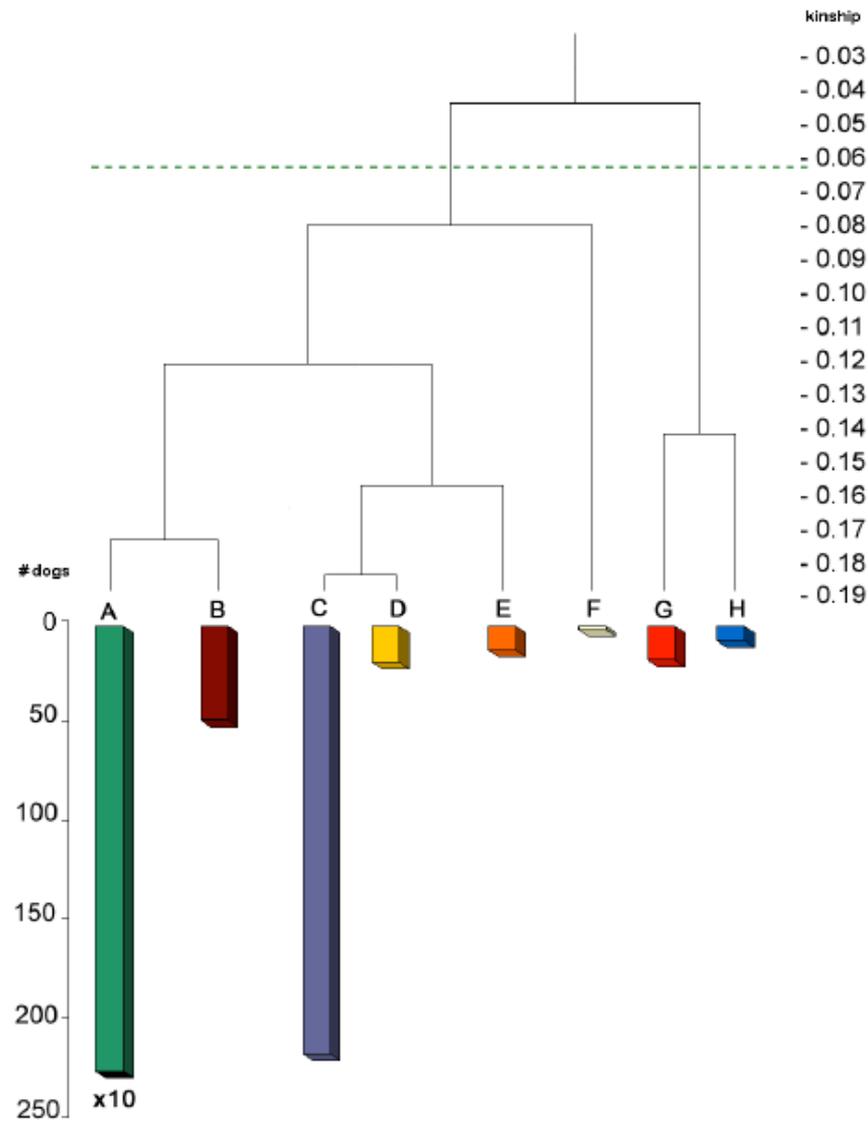


Figure 6
Cluster analysis of current population (all-gen-tree). Results of clustering based on kinship coefficients calculated using the tabular method (all generations included); the legend with codes per cluster was added in order to compare this dendrogram to that in Figure 7; the length per cluster corresponds with the number of (reproductive) individuals, except for cluster A, which is 10 times the size depicted, representing 2236 animals; the line at the 0.0625 kinship level, corresponds with the 'cut-off level' of the cluster analysis of Figure 7

A key thing Icelandic Sheepdog breeders learned from this analysis was that animals they had been choosing for import based on pedigree analysis to improve genetic diversity belonged to the same cluster they were trying to improve. This of course was because too few generations of pedigree data were used to reveal the early inbreeding in the closed population of the breed.

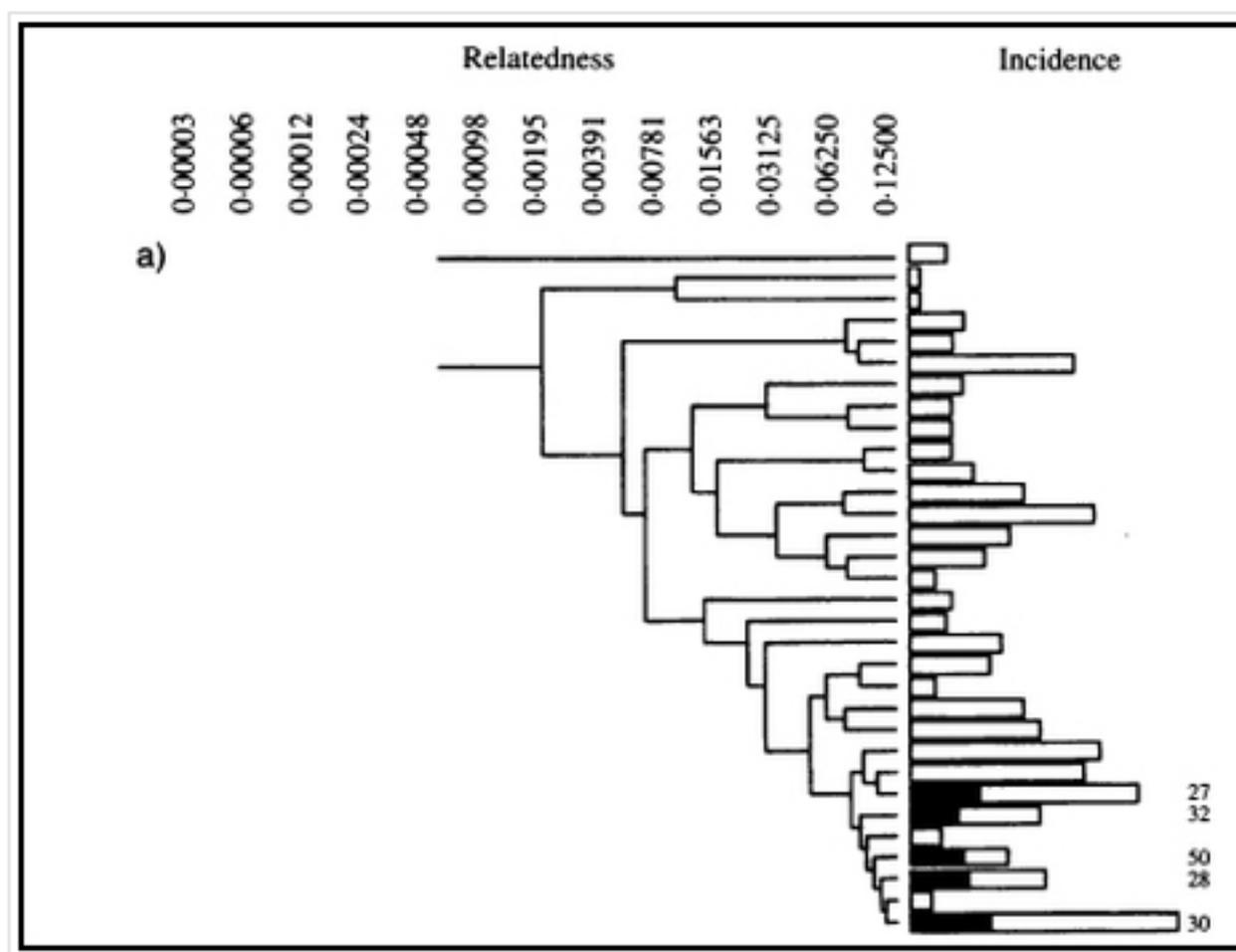
The dendrogram clearly identifies the animals that are genetically valuable from those that are not. Most of the breed's population (88%) belonged to the "green group". By sheer numbers along, these animals are genetically the least valuable in the breed and all other things being equal should be the lowest priority for breeding. On the other hand, the groups with the smallest numbers of members (e.g., yellow, blue, orange), and those more distant from the main group (based on branch lengths; e.g., red and blue) are genetically most valuable and are the highest priority for breeding to prevent loss of these lines.

The value of cluster analysis

How could breeders use this information? The analysis showed that although no single cluster contained all potential diversity, the genetic diversity of the entire population could be improved slightly (from 2.2 to 4.7) by judicious use of animals in the various clusters. Breeders could also use the cluster diagram to explore breeding options that would avoid pairing genetically similar animals. Monitoring the sizes of these clusters over time would provide breeders with an overview of the genetic structure of their breed at a particular time that would be easy to understand, and actions could be taken early to prevent excess representation of some genetic lines and potential loss of others.

Another really useful way we could be using kinship information is to identify the "sources" of genetic disorders.

Here is another dendrogram based on kinship, this time for a breeding colony of Labradors managed by a Dutch guide dog organization. All animals were screen for elbow dysplasia, and affected animals represented by the solid portions of the bars of the graph.



From this analysis, it was immediately clear that all the cases of elbow dysplasia fell into just a few close clusters (the partially dark bars). It wasn't necessary to know anything about the genetic basis of the problem, or the genetics of the animals except what could be inferred from pedigree analysis. This could be an amazingly powerful way to monitor genetic disorders in dogs, and would require nothing more than an up-to-date pedigree database and the relevant information about the health issue. It would be easy to do. (Read more about it [HERE](#).)

Inbreeding & Kinship

You'll need to correctly answer at least **12 of the 17** questions below (**at least 70%**) to progress to the next unit.

Question #1 - The more offspring an animal has, the _____ its mean kinship.

- > higher
 - > lower
-

Question #2 - A dog's coefficient of inbreeding is equal to its mean kinship.

- > True
 - > False
-

Question #3 - The higher the kinship coefficient of a pair of animals, the more closely related they are.

- > True
 - > False
-

Question #4 - In a population of animals, the ones with the highest mean kinship are genetically most valuable.

- > True
 - > False
-

Question #5 - The kinship of two dogs that share the same parents is

- > 0%
 - > 10%
 - > 25%
 - > 50%
 - > 100%
-

Question #6 - It is possible for two highly inbred dogs to produce offspring with a COI of 0%.

- > True
 - > False
-

Question #7 - The best way to determine if a breed has genetic structure or "lines" is by analyzing

- > coefficient of inbreeding

- › kinship
 - › population size
 - › phenotype
-

Question #8 - You can produce puppies that will have high genetic value to the breed by choosing a dam and sire with low kinship.

- › True
 - › False
-

Question #9 - A graph of all possible pairwise kinship values in a population will show you the lowest and highest inbreeding coefficients you could produce in a breeding.

- › True
 - › False
-

Question #10 - A dog can have a low COI but a high mean kinship.

- › True
 - › False
-

Question #11 - A dog can have a high COI but a low mean kinship.

- › True
 - › False
-

Question #12 - A dog can have much to offer the breed in terms of type but have a low genetic value in terms of the population genetics of the breed.

- › True
 - › False
-

Question #13 - The "genetic structure" of a dog breed refers to the helical structure of canine DNA.

- › True
 - › False
-

Question #14 - Cluster analysis identifies groups of dogs with similar inbreeding coefficients.

- › True
 - › False
-

Question #15 - Of the clusters B, E, F, and G, which has the highest genetic value as we've defined it?

- > B
 - > E
 - > F
 - > G
-

Question #16 - With information about kinship, breeders could identify the emergence of a new inherited disorder when only just a few cases have been reported.

- > True
 - > False
-

Question #17 - Dogs with the highest risk of producing genetic disorders in their offspring have the lowest kinship.

- > True
 - > False
-

[« Previous Unit](#)

[Next Unit »](#)

 August 14, 2015  carol beuchat  Edit

Consequences of Inbreeding

At the beginning of the course, we talked briefly about the advantages and disadvantages of inbreeding. You'll remember this list:

ADVANTAGES

- › *increased uniformity*
- › *increased prepotency (ability to pass on traits to offspring)*
- › *"fixing" of desired traits and breed type*

DISADVANTAGES

- › *lower fertility*
- › *lower "vigor"*
- › *birth defects*
- › *smaller size*
- › *fewer offspring*
- › *slower growth*
- › *higher offspring mortality*
- › *shorter lifespan*
- › *increase in genetic diseases*
- › *reduced "genetic potential" (ability to improve a trait)*

Why does inbreeding increase uniformity and prepotency?

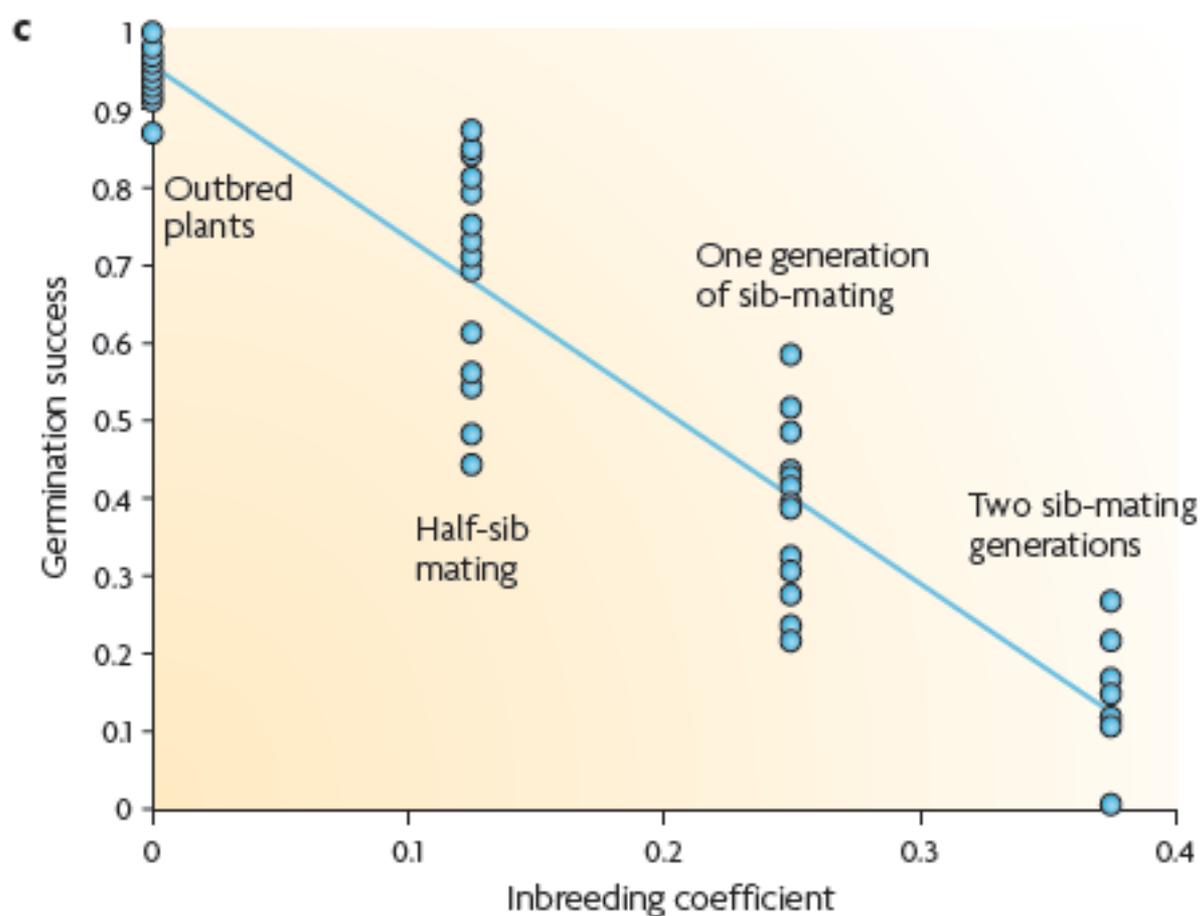
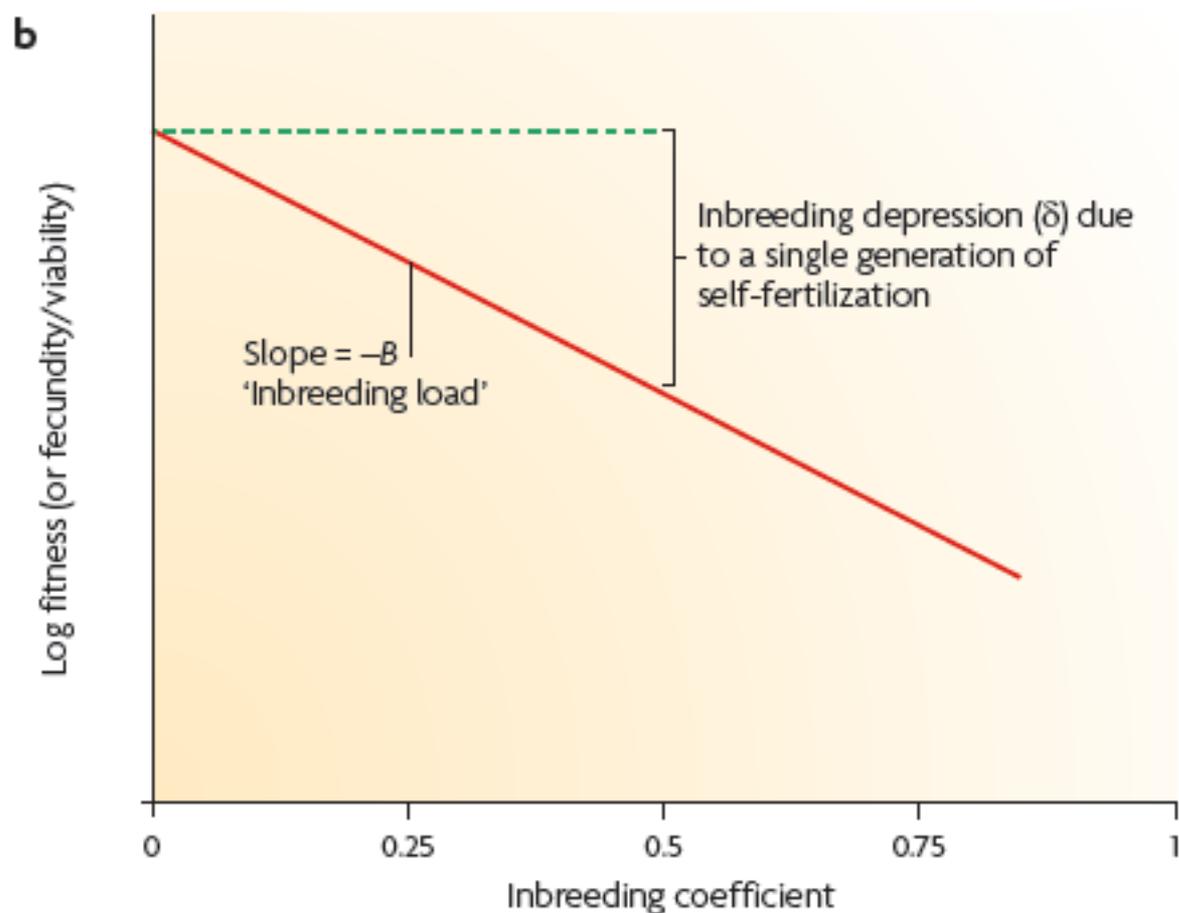
Inbreeding increases homozygosity. By that, we mean that if there are two (or more) alleles in the population for a gene, the frequency of AA and aa will increase, and Aa and aA will decrease. If a dog is homozygous for AA, then it can ONLY pass the A allele on to its offspring - it is "fixed" for the A gene. The greater the degree of homozygosity of an animal's genome, the more uniform its offspring will be because they will all get the same allele for many genes from that parent. If you are trying to breed for specific traits, this is a huge advantage. Variation among litter mates will be reduced, and the inbred parent will be said to be "prepotent" - it creates offspring with a recognizable "look".

This would all be good except that nature doesn't especially like homozygosity. In hundreds of studies, in many different species both plant and animal (including domestic animals), there is irrefutable evidence that homozygosity comes with a price. Wright noted that

“...it may be readily shown that the decrease in vigor in starting inbreeding in a previously random-bred stock should be directly proportional to the increase in the percentage of homozygosity”, and “As for the other effects of inbreeding, fixation of characters and increased prepotency, these are of course in direct proportion to the percentage of homozygosity.”

This is illustrated in these figures. "Fitness" is a measure of an animal's ability to produce offspring that can contribute genetically to the next generation. Producing offspring that don't themselves produce offspring gives you a fitness of zero. It might be that the offspring are infertile, or died after birth, or were too slow or too stupid to outrun a predator - doesn't matter, the measure of interest is

whether an animal's genes will stay in the gene pool through the next generation.



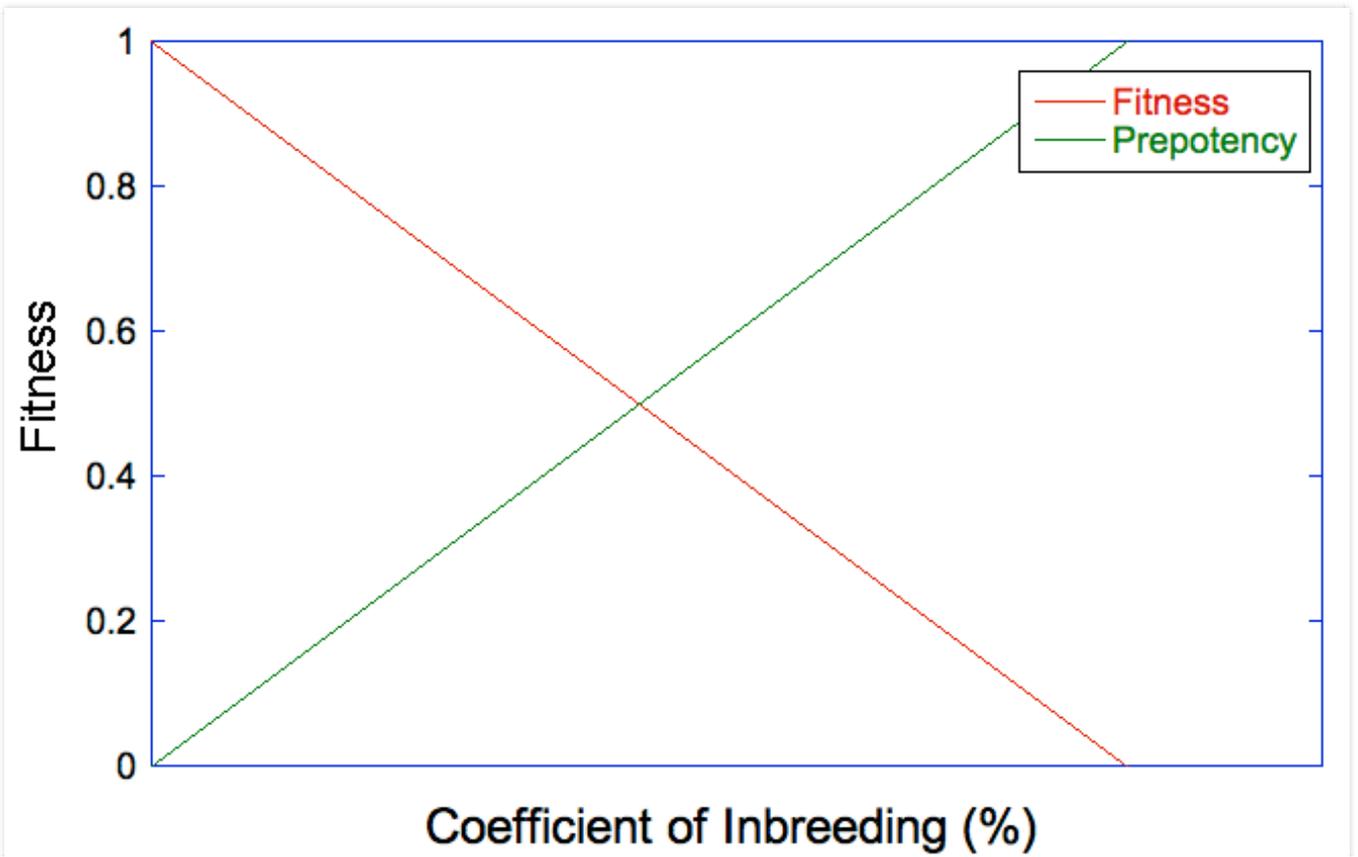
Inbreeding reduces fitness (the red line), and the decrement in fitness is proportional to the degree of inbreeding. This reduced fitness is called "inbreeding depression", which is a catch-all for all things that play a role in reducing fitness. If you start with an outbred plant (so high heterozygosity) that self-pollinates (self-fertilization, so we don't have to worry about the genetics of the mate), germination of the seeds produced will be reduced. As you continue to self-pollinate successive generations, the reduction in germination is proportional to the inbreeding coefficient and therefore the amount of homozygosity (blue line).

This is a very handy relationship. The cost and benefit of inbreeding are directly proportional to the COI. This means that a breeder can choose a level of inbreeding that is a good balance between cost and benefit.

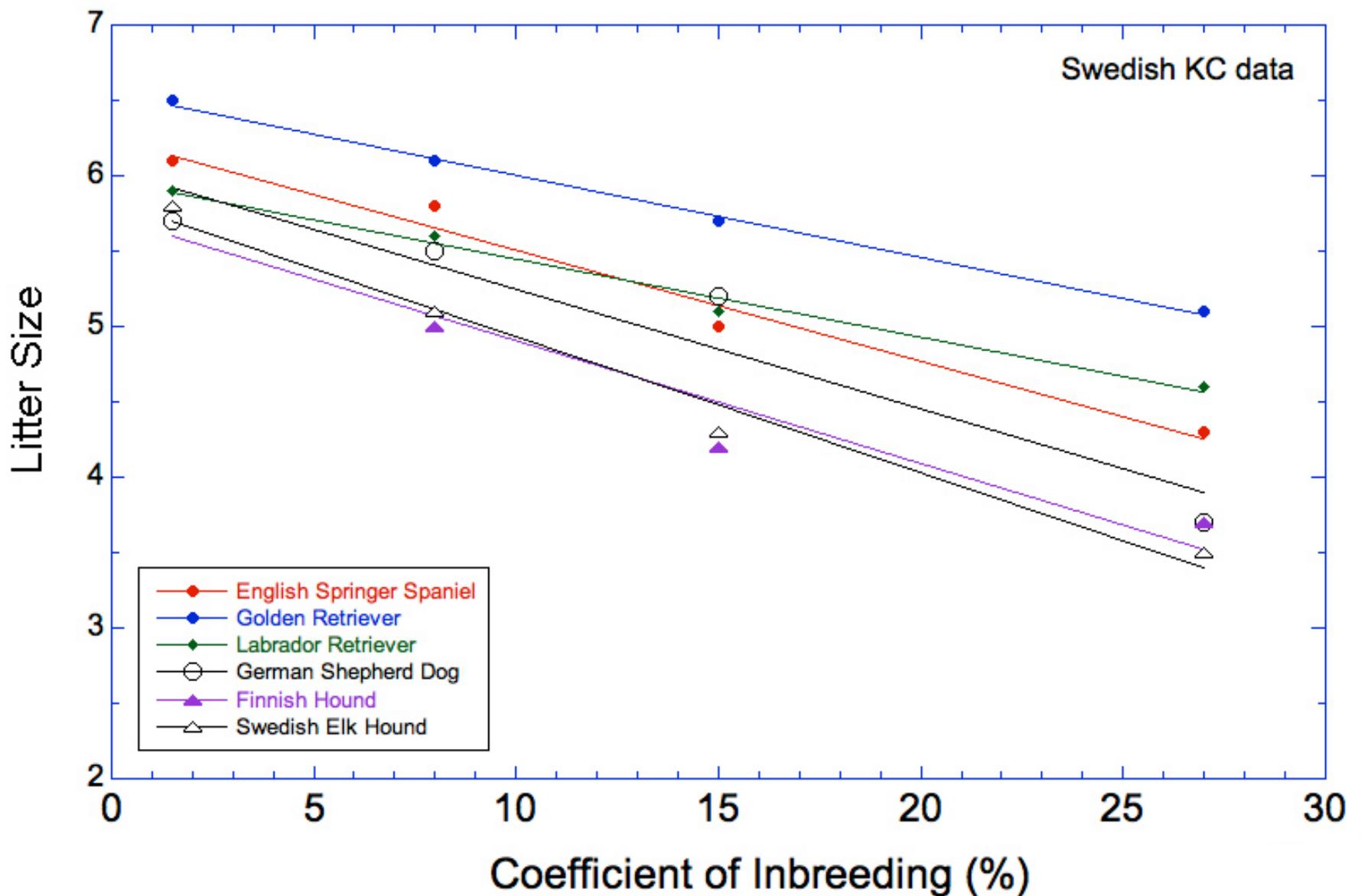
Inbreeding depression in dogs

Are there data that show a negative effect of inbreeding depression in dogs?

Here are some data on litter size of 6 breeds of dogs from the records of the Swedish Kennel Club. The first thing I would warn about is that these are probably 10 generation COIs, which we already know are likely to underestimate the true COI especially for breeds that have been around for a while (e.g., Golden Retrievers and Labradors). So understand that the placement of these lines relative to each other and the X axis is not likely to be the "truth".



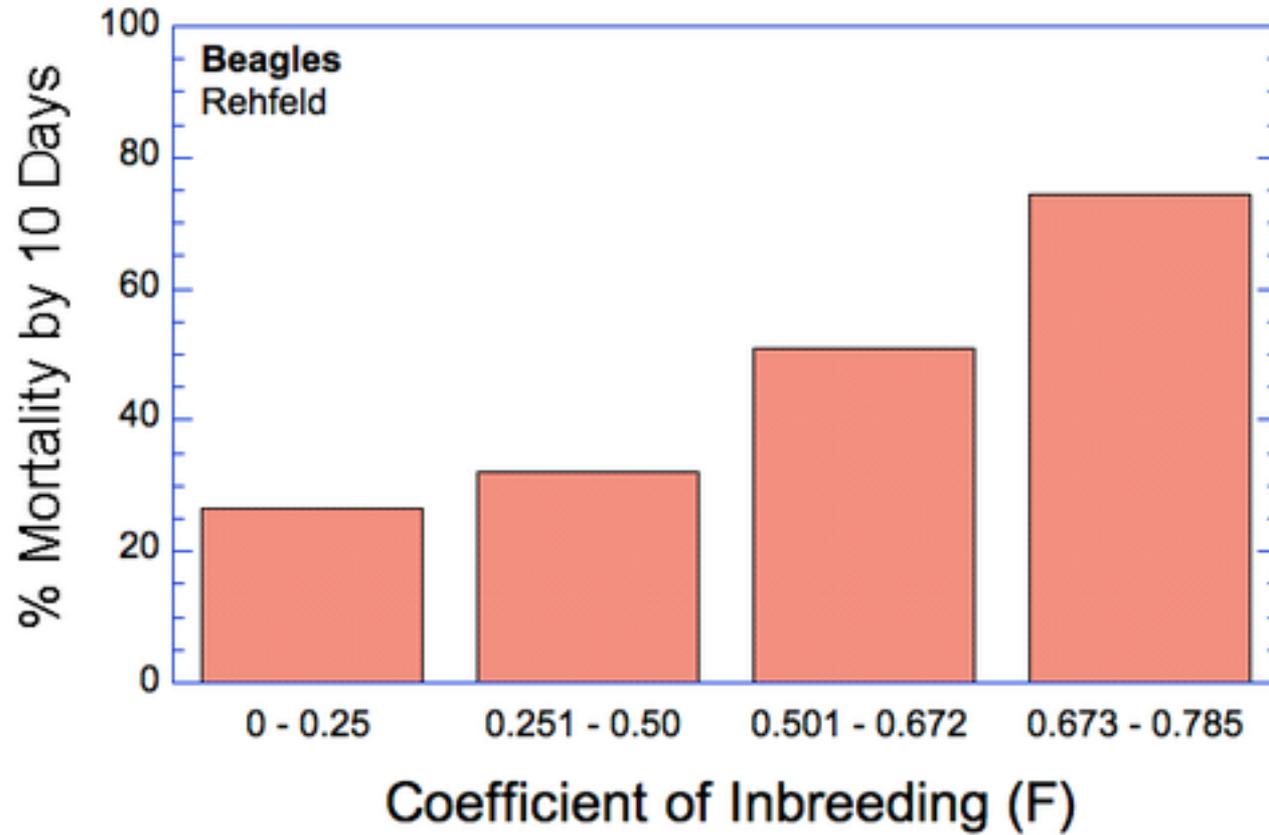
When the COI is zero, fitness is at its maximum and prepotency and uniformity are at their lowest. As inbreeding increases, variation in the offspring goes down but so does fitness.



For our purposes, however, it doesn't really matter. What we want to see is the effect of COI on litter size, and as observed by Wright and many others, the reduction in litter size as inbreeding increases is linear.

The slopes of these lines tell us exactly what this "cost-benefit" ratio is. For these breeds, those slopes are about 0.1, which means that an increase in inbreeding of 10% reduces litter size by about 1. If normal litter size is about 6, a COI of 30% - which is not uncommon in many breeds - would reduce the litter size by HALF. That is half as many offspring from which to choose your "pick", and on top of this realize that these puppies will have reduced fitness in the ways noted by Wright - they are likely to be smaller, less vigorous, have more birth defects and higher mortality, grow more slowly, have shorter lifespan, and of course increased incidence of genetic disorders caused by recessive mutations.

How is inbreeding depression manifested in offspring? The impact on puppy mortality is clear. These data for Beagles unfortunately pool together all the dogs with COI less than 25% (so we can't see whatever effect there is, but the average mortality by 10 days for this group was greater than 20%. As inbreeding increases above 25%, the mortality increases, to about 30% for dogs with COI between 25-50%, and higher still as COI increases.



In Standard Poodles, dogs with inbreeding less than 6% live 4 years longer than those with higher COI.

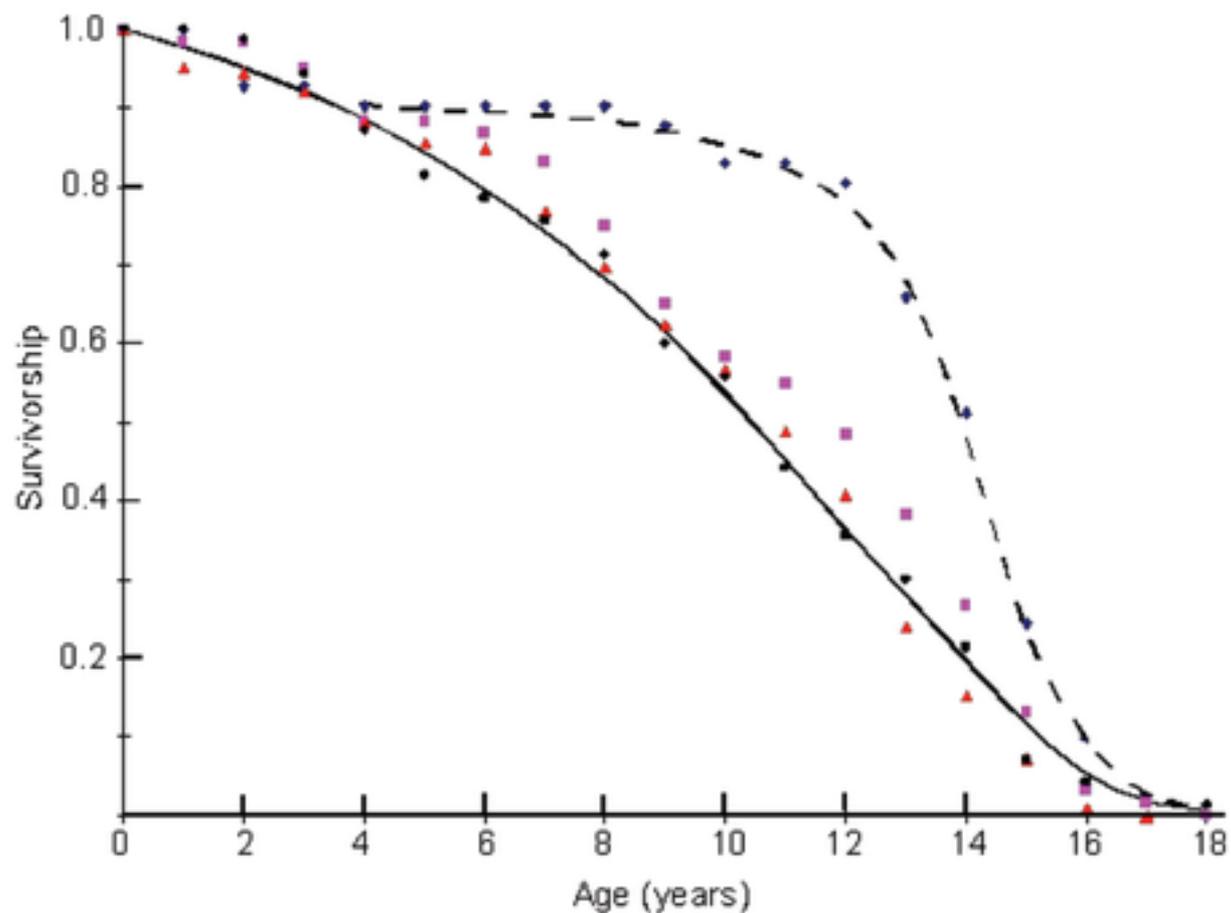


Fig. 3. Standard Poodle survivorship at different levels of inbreeding. Blue diamonds: < 6.25% (N=39); pink squares: 6.25%-12.5% (N=65); red triangles: 12.5-25% (N=141); black circles: > 25% (N=71). The solid line is fitted to the > 25% group.

Also in Poodles, there was a relationship between COI and mortality from bloat. The risk of bloat is roughly proportional to the increase in COI. For example, a COI of 30% elevates the risk of bloat by more than 30%.

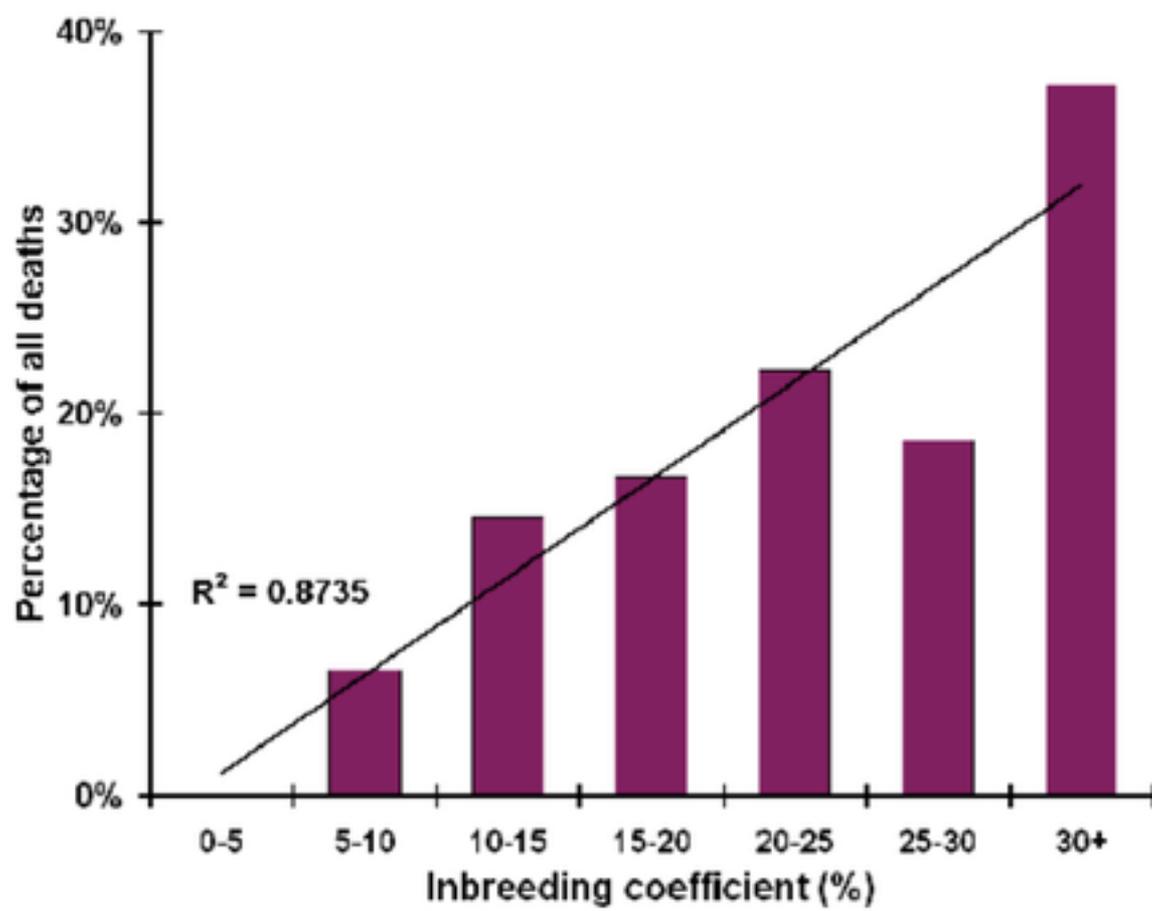
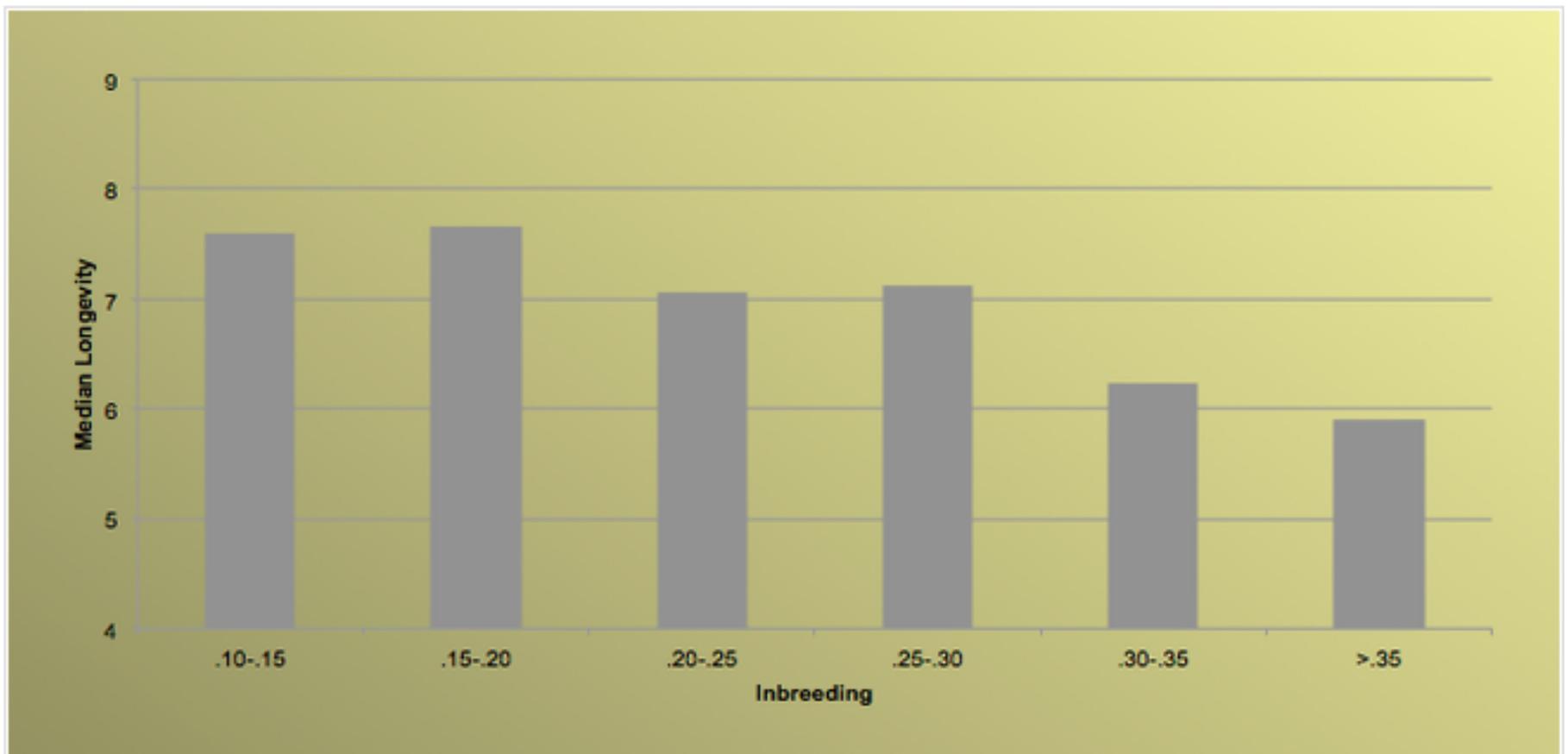


Fig. 4. Percentage of dogs in a particular inbreeding range that were reported as dying of bloat.

In Bernese Mountain Dogs, each 10% increase in COI reduces lifespan by 200 days. For a dog with COI of 30%, that's a reduction in lifespan of almost *two years*.



How much inbreeding is "necessary"?

So now you're probably thinking that you're stuck between a rock and a hard place. Inbreeding is necessary to fix type and without it purebred dogs wouldn't exist. Is that true? We'll talk about that next.

Have you completed this unit? Then mark this unit as completed.

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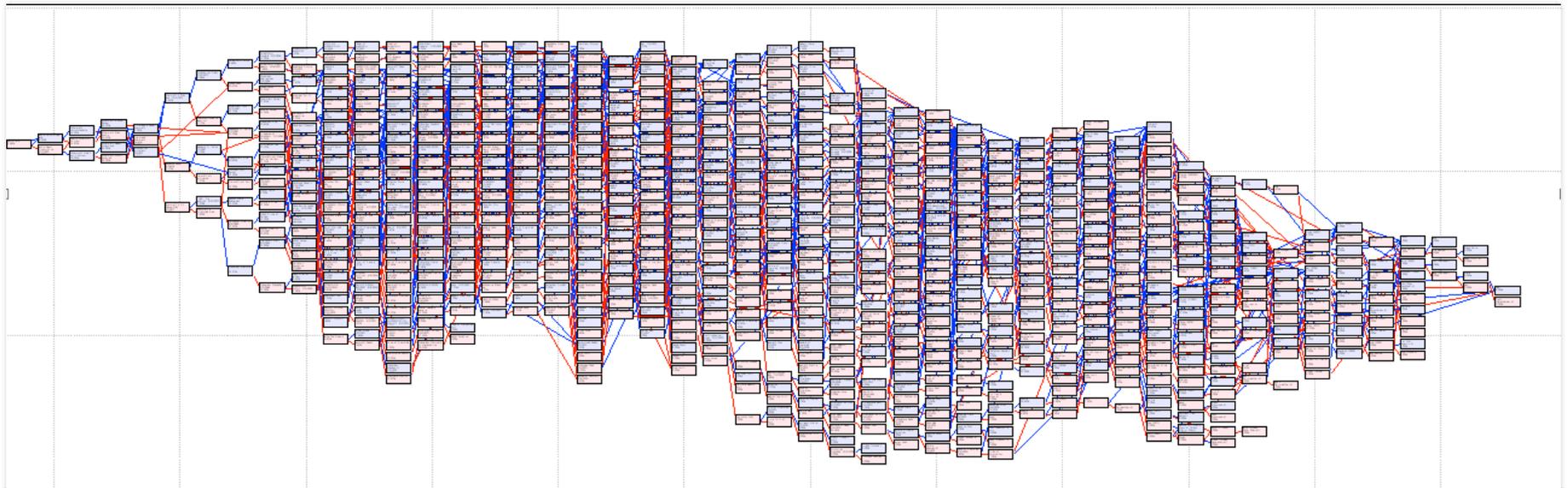
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Managing Inbreeding

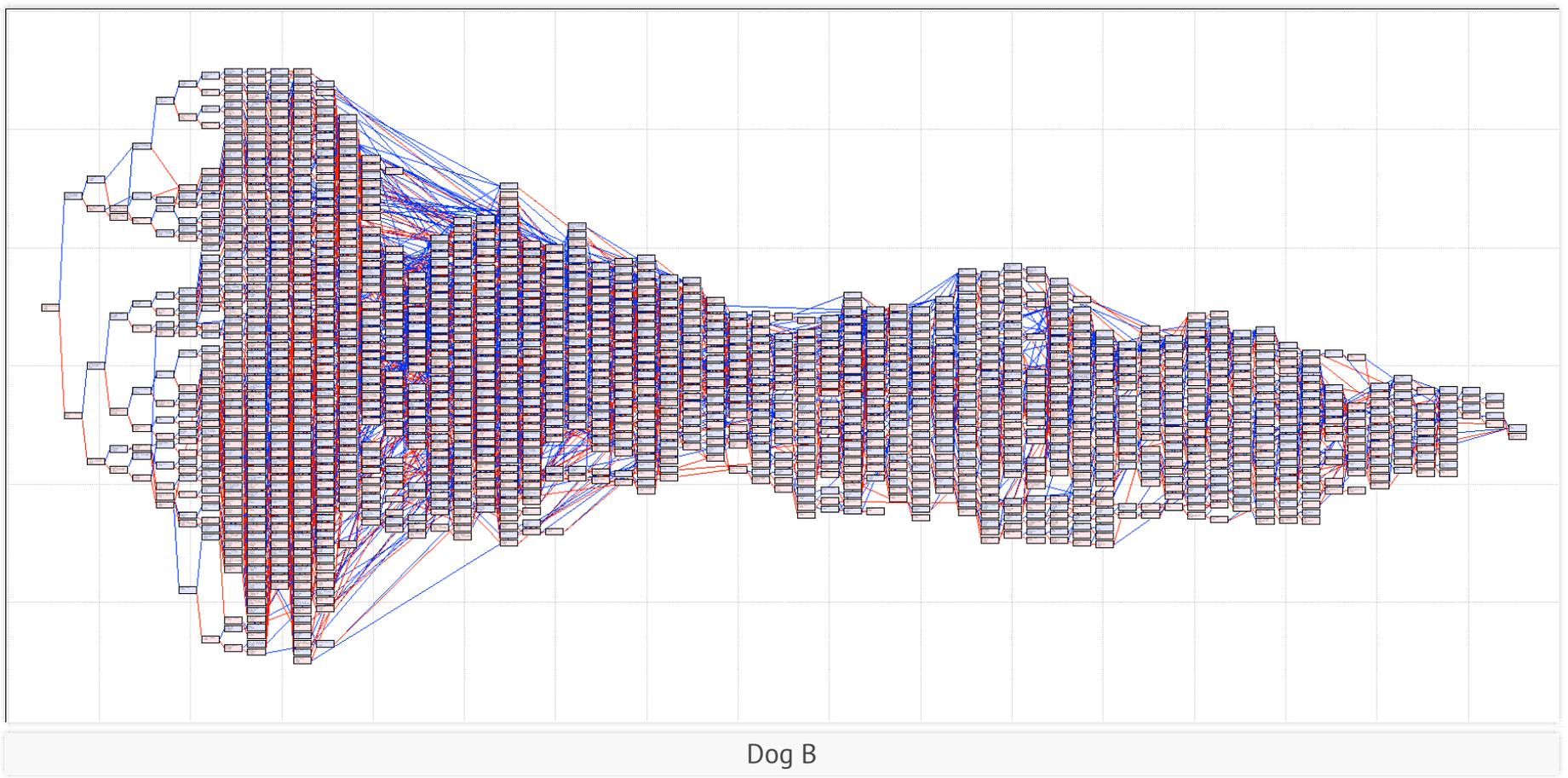
Now that you understand both the costs and benefits of inbreeding, you probably would like to reduce the COI of the litters you breed, but the gene pool of your breed is small and your options are therefore limited. The age-old strategy to improve the vigor of an inbred line is to bring in an "outcross", by which we mean a dog of the same breed but not closely related. How could you do this?

Here are the pedigrees of two dogs of the same breed. The dog of interest is on the left, and its ancestors by generation go to the right, to the earliest dogs in the pedigree database. In these charts, each dog is represented only once, so dogs with multiple matings will have more than one line connecting them to descendants. Blue boxes are males, pink are female. You can click on each one to see a larger version.

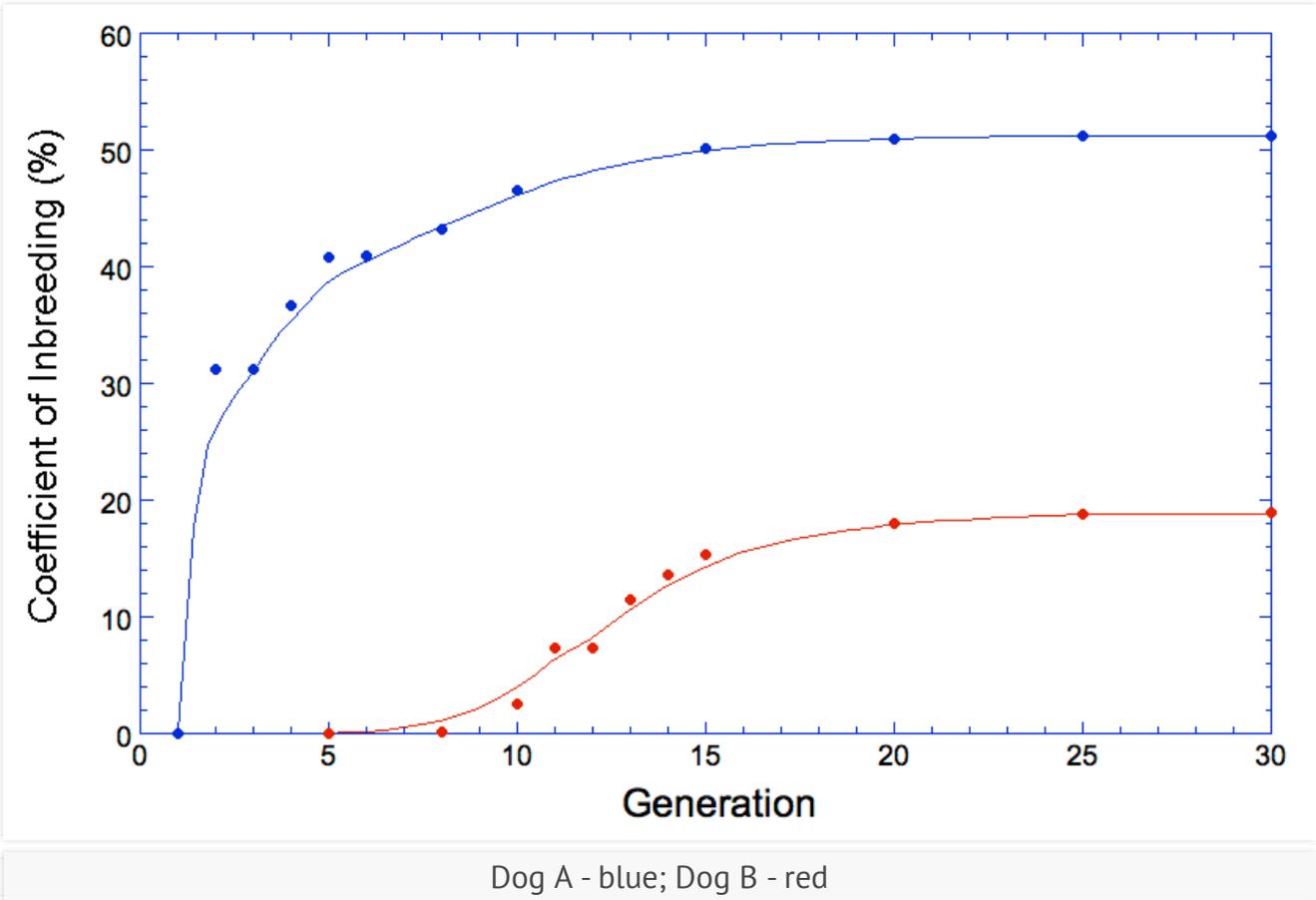
If you look at the origin of the two pedigrees below, you will see that the two dogs had the same early history. The one at the top (Dog A) has been very tightly inbred for the last few generations. Dog B on the other hand, is the offspring of two dogs who share no ancestors for the previous 5 generations, so (relatively speaking) this is an outcross. Because a population of dogs loses genes every generation both as a result of selection and also genetic drift, these two lines of dogs that have been separate for a few generations will have diverged genetically. The difference might not be huge, but there will be some restoration of heterozygosity in the breeding, which should have a positive effect on inbreeding depression and health.



Dog A



The difference in recent breeding history of Dogs A and B shows up clearly in the graph of coefficient of inbreeding by generation. Dog A is the offspring of two closely related dogs, and that is reflected in the high COI even one generation back. By 10 generations, the level of inbreeding is over 45%. Because no common ancestors appear in the pedigree of Dog BN for 5 generations, the COI doesn't begin to increase in its pedigree until about generation 10. The pedigree of Dog B is less complete than that of Dog A, and missing animals will artificially reduce the calculated COI, so it isn't safe to assume that the COI of B stays as low as appears in this graph. (And the pedigree of Dog B is also much deeper, which will matter as well.) But Dog B will definitely benefit genetically from the lack of shared ancestors in its recent history.



This strategy of managing subgroups of animals within a breed that can be used for outcrossing is the most effective way to minimize the loss of genetic diversity over time and mitigate the effects of inbreeding. Even if these separate populations are being selected for the same traits, they will diverge genetically over time. This provides an opportunity to outcross for the benefit of improv-

ing genetic health while still maintaining type and the other traits that are under selection. Most commercially bred animals are managed this way, not only at a local scale but even internationally. Certainly this is possible for dog breeders with relatively small breeding programs to do this if groups of breeders can coordinate efforts and inbreed strategically for the purpose of producing a group of animals that can be used for outcrossing. The overall level of genetic diversity in the breed will be higher and a regular program of outcrossing to a subpopulation will stabilize health and minimize the accumulation of effects of inbreeding depression.

Please also visit the ICB website and read the post about "[Using Inbreeding to Manage Inbreeding](#)", which follows nicely from this lesson.

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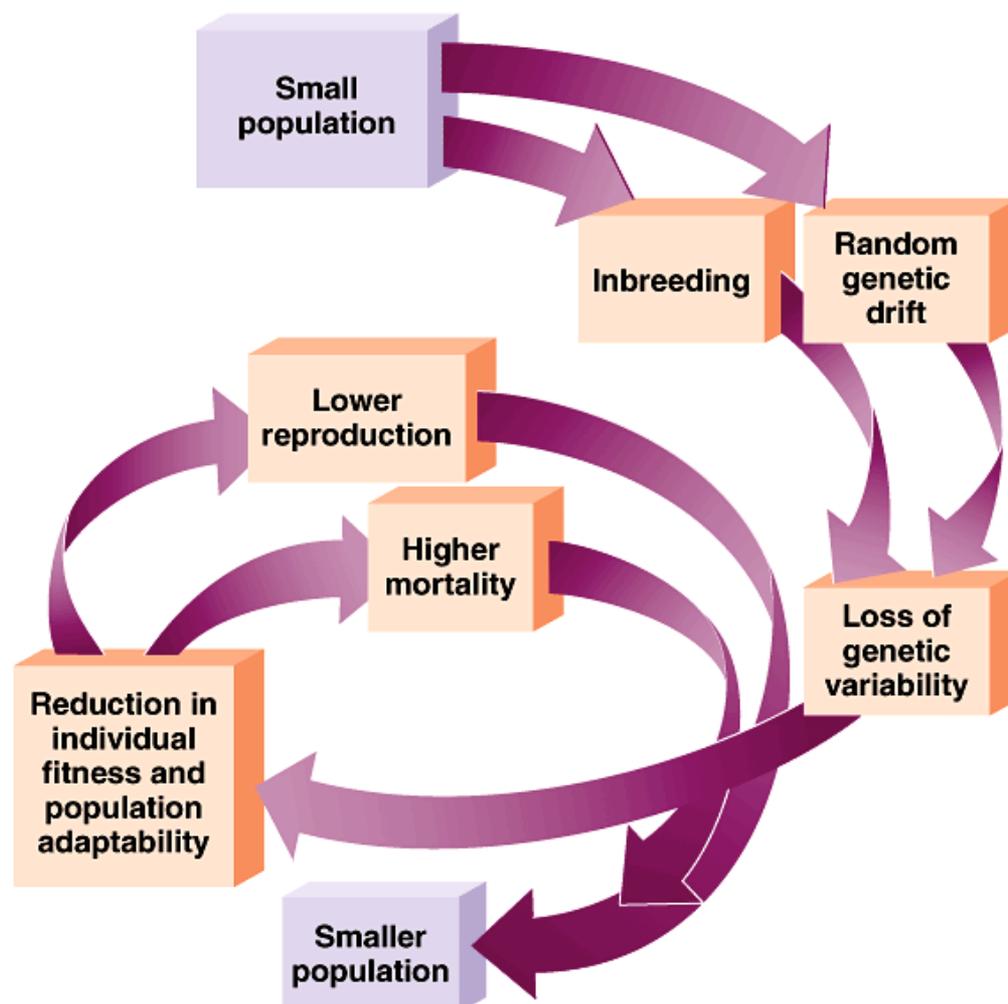
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Putting it all together

Historically, dog breeders have failed to take advantage of coefficient of inbreeding as a way to evaluate the best options for parents of a litter. There seems to be a general understanding that lower is better, but how low is "good", or how high is "bad" are both usually a matter of opinion. Rarely are the benefits and costs of inbreeding considered together as very real tradeoffs that will manifest in the litter. More often, COI is computed using too few generations of pedigree data, and the resulting "low" COI is held up (along with "health tested") as a measure of quality. This seems like such a waste. If breeders care about the quality of the puppies they produce, it makes little sense to do all relevant health testing then breed a litter with a COI of 37%. That's not responsible breeding. It's a very high level of risk for the individual puppies, and it contributes to the feedback loop of the "extinction vortex" that little by little chips away at the genetic foundation of a breed until there aren't any healthy animals left.



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Don't make the mistake of thinking that your breed is popular and numerous and therefore doesn't have the "small population" problem that is a component of the extinction vortex. The true population size is not the absolute number of animals in a breed, but the number that are *actually being bred*, which in most breeds is less than 25%. And most of those dogs are related to each other (and in some cases *highly* related), so the number of breeding animals in terms of genetics is smaller still. In the [Nova Scotia Duck Tolling Retriever](#), which has a global population in the thousands, the entire breed is the genetic equivalent of only 2 dogs that are as closely related as full sibs (!!!). The global population of registered [Afghan hounds](#) is about 7,000 dogs, but in terms of genetic diversity the breed is down to about 9. The worldwide population of [Standard Poodles](#) numbers in the tens of thousands, but genetically the

breed probably has fewer than 200 animals. On top of the small number of "genetic animals" in these breeds, the average level of inbreeding is high. These are the ingredients for genetic disaster.

When wild animals face diminishing population size and low genetic diversity, geneticists and biologists evaluate the status of the species or population and formulate a plan to prevent extinction. The field of conservation genetics developed out of these efforts, and the same tools used to genetically rehabilitate wild animals can be used to improve the genetic status of purebred dog breeds. But this will require first understanding the true genetic status of the breed, then forming a group of breeders that agree to cooperate in the implementation of breeding strategies to improve the genetic health of the breed. If they can do this, both dogs and breeders will win.

Using COI for genetic management

You'll need to correctly answer at least **19 of the 27** questions below (**at least 70%**) to progress to the next unit.

Question #1 - Inbreeding is a property of

- > a population
 - > an individual
 - > both individuals and populations
-

Question #2 - The COI can indicate the prepotency of a dog.

- > True
 - > False
-

Question #3 - The best way to produce research animals with specific genetic disorders caused by recessive mutations is by close inbreeding.

- > True
 - > False
-

Question #4 - In the 10th generation of a dog in which there has been no inbreeding, there will be more than 1,000 ancestors.

- > True
 - > False
-

Question #5 - Which of these is NOT a useful way to control the rate of inbreeding in a purebred dog breed?

- > Maintain a large population size
- > Encourage random breeding within the entire breed population
- > Increase the percentage of dogs that are bred
- > Maintain inbred subgroups within the breed

Question #6 - Kinship is a measure of

- › similarity in genotype
 - › similarity in phenotype
 - › the number of generations of inbreeding of a dog
-

Question #7 - Highly inbred animals should not be used for breeding.

- › True
 - › False
-

Question #8 - Which of these is NOT true of a breed's founders?

- › All have a coefficient of inbreeding of zero.
 - › They are the first registered members of a recognized breed.
 - › They are usually ancient and unknown.
 - › They define the initial genetic diversity of the breed's gene pool.
-

Question #9 - A dog has two alleles, Aa, at a locus. The probability of a daughter inheriting the allele "A" is 0.25.

- › True
 - › False
-

Question #10 - Two alleles at a locus that are homozygous by descent both came from an ancestor shared by the dam and sire.

- › True
 - › False
-

Question #11 - A dog has two alleles, Aa, at a locus. The probability of a granddaughter inheriting the allele "a" is 0.25.

- › True
 - › False
-

Question #12 - One way to manage inbreeding is to use fewer generations in the computation of COI.

- › True
 - › False
-

Question #13 - In each generation of a pedigree, the potential number of ancestors

- › doubles
 - › triples
 - › increases by $(0.5)^n$
-

Question #14 - COI calculated using incomplete pedigree data will result in

- › an overestimation of the true value
 - › an underestimation of the true value
-

Question #15 - Choosing a sire that has a low COI will reduce the probability of genetic defects in the puppies.

- › True
 - › False
-

Question #16 - The dogs in your breed that have the highest "genetic value" will have the

- › highest mean kinship.
 - › lowest mean kinship.
 - › highest coefficient of inbreeding.
 - › lowest coefficient of inbreeding.
 - › highest number of offspring.
-

Question #17 - You can locate the source of a genetic problem in a breeding without needing DNA information by using

- › You can locate the source of a genetic problem in a breeding without needing DNA information by using
 - › coefficient of inbreeding in a dendrogram.
 - › kinship coefficient in a cluster analysis.
-

Question #18 - All puppies in a litter will have the same coefficient of kinship.

- › True
 - › False
-

Question #19 - The kinship of a sire and dam is proportional to the risk of producing a puppy with a genetic disorder caused by a recessive mutation.

- › True
 - › False
-

Question #20 - In a dog with a coefficient of inbreeding of 30%, which of these is likely to be true?

- › 30% of its genome is homozygous.
 - › 70% of its genome is homozygous.
 - › It doesn't tell you anything about homozygosity of the genome.
-

Question #21 - An animal with higher "fitness"

- › is more likely to be fertile
 - › is the fastest and most agile.
 - › is more likely to suffer a seizure disorder.
-

Question #22 - Let's say you're shopping for a new puppy and have two choices. Indicate which puppy you would choose.

- › Puppy A has a COI (calculated to founders) of 8% but no health testing.
 - › Puppy B has a COI of 31% (to founders) but was clear for the 3 DNA tests available for the breed.
-

Question #23 - Inbreeding reduces litter size in dogs.

- › True
 - › False
-

Question #24 - Inbreeding can reduce the expected lifespan of a dog by years.

- › True
 - › False
-

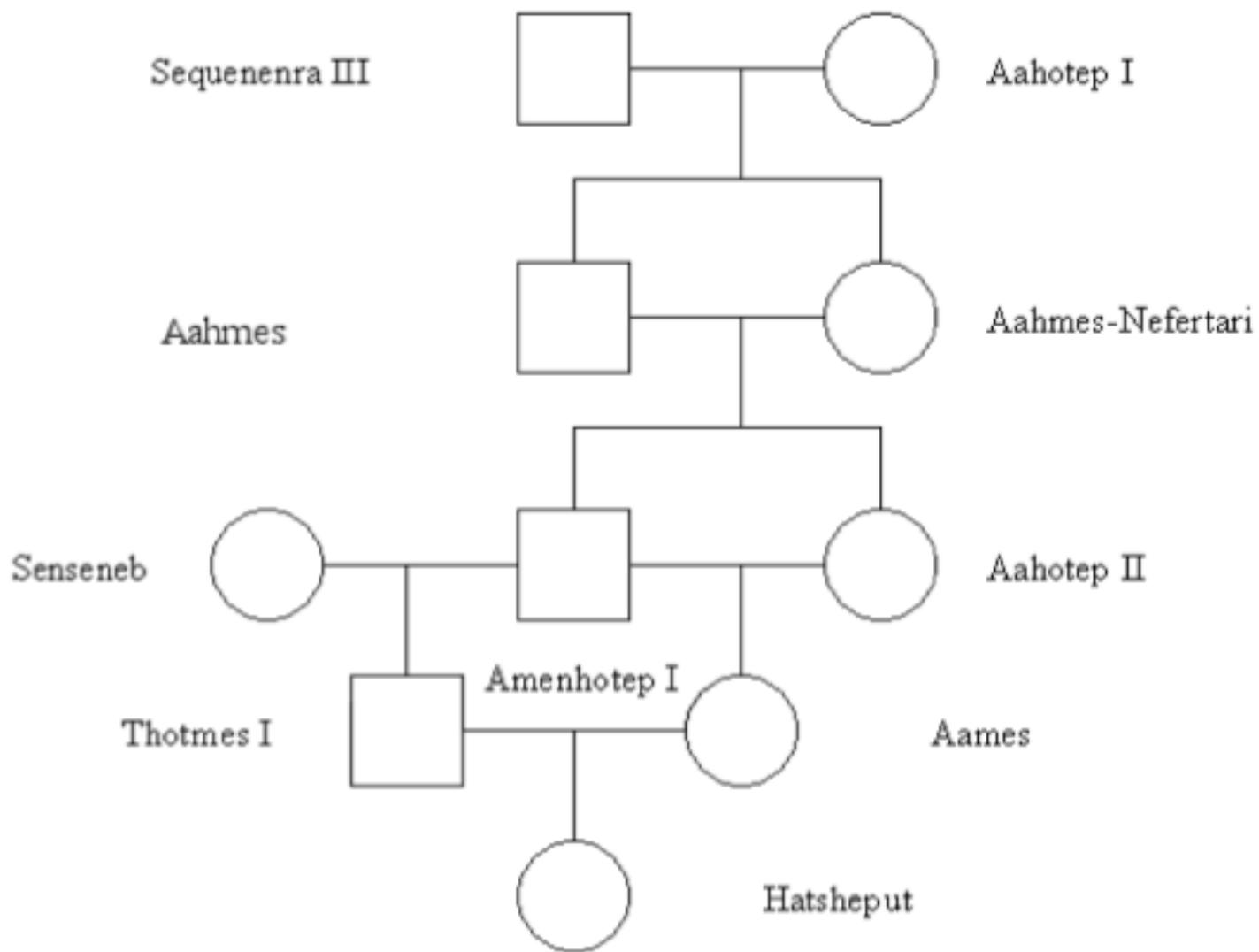
Question #25 - In some breeds, inbreeding increases the risk of bloat.

- › True
 - › False
-

Question #26 - As prepotency increases, fertility goes down.

- › True
 - › False
-

Question #27 - This is the pedigree of Hatsheput, the 5th pharaoh of the Eighteenth dynasty of ancient Egypt, and she is regarded by many scholars as one of the most successful pharaohs. From her pedigree, identify which individual is most inbred (ie highest COI).



- > Aames
- > Aahotep II
- > Aahmes
- > Thotmes I
- > Hatsheput

« Previous Unit

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