FACULTEIT DIERGENEESKUNDE
accredited by EAEVE

DEPARTMENT OF VETERINARY AND BIOSCIENCES

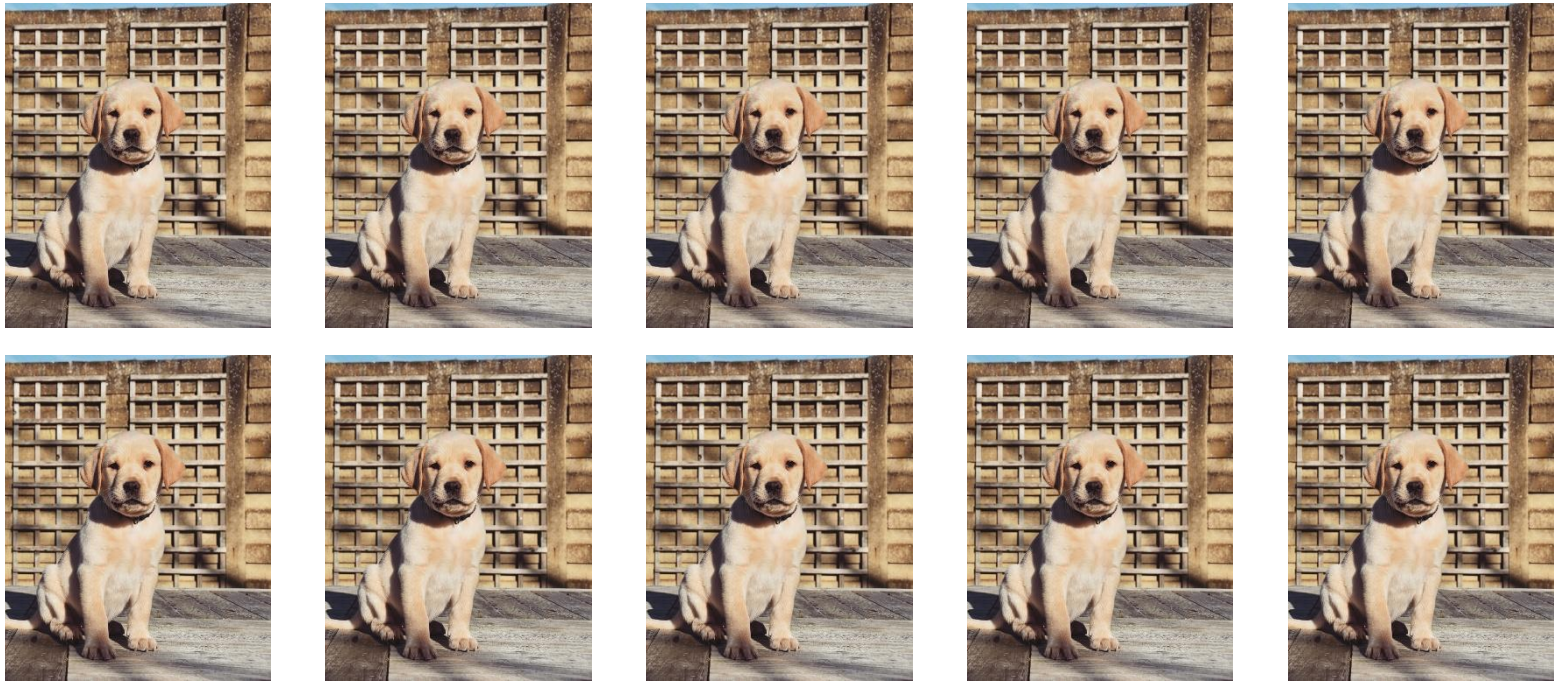
LABORATORY OF ANIMAL GENETICS

Strategies for genetic diversity

Prof. dr. Bart Broeckx

Situation in Belgium

- Back in 2018:
  - 60% of the puppies that start the training are rejected



Bogaerts et al. (2019)

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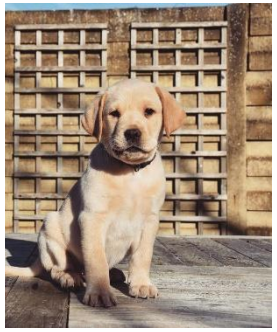

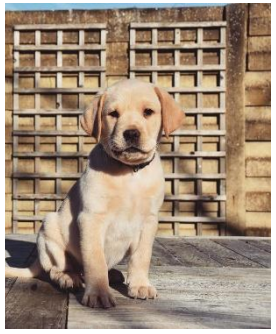

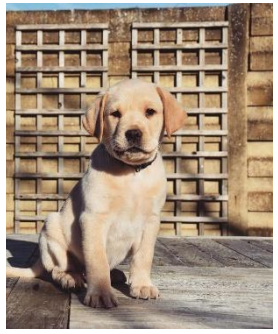

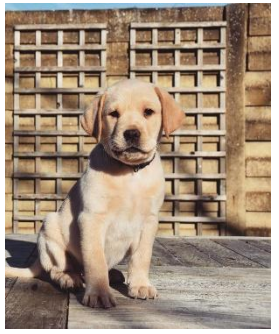

Bogaerts et al. (2019)

Situation in Belgium

- Back in 2018:
  - 60% of the puppies that start the training are rejected
  - Average cost of a rejected dog

≈ 10 000 euro

Major problem!

Why was the success rate that low?

Why was the success rate that low?

- Causes:
  - Orthopedic disorders
  - Behavioural rejections

⇒ Characteristics with a genetic basis

Solution?

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- Observation:
  - All these characteristics (behaviour, joints) are heritable

“you look like your family”

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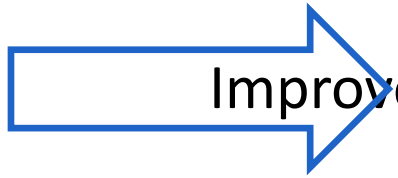
⇒ Improve the parents  Improved puppies

IT MAKES ONE THINK!

Purpose Dogs VZW

Purpose Dogs VZW

- Non-profit organization
- Founded in 2018
- Breed our own dogs

Challenges

- Reduction of the number of rejections
- Avoid other disorders to pop up
- Grow to meet the demand

Practically:

- Improved joints
- Better suited behaviourally
- Focus on genetic diversity

Challenges

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Practically:

- Improved joints
- Better suited behaviourally
- Focus on genetic diversity

Selection of part of the population

vs

Increase of the number of dogs in the program

Challenges

- Reduction of the number of rejections
- Avoid other disorders to pop up
- Grow to meet the demand

Practically:

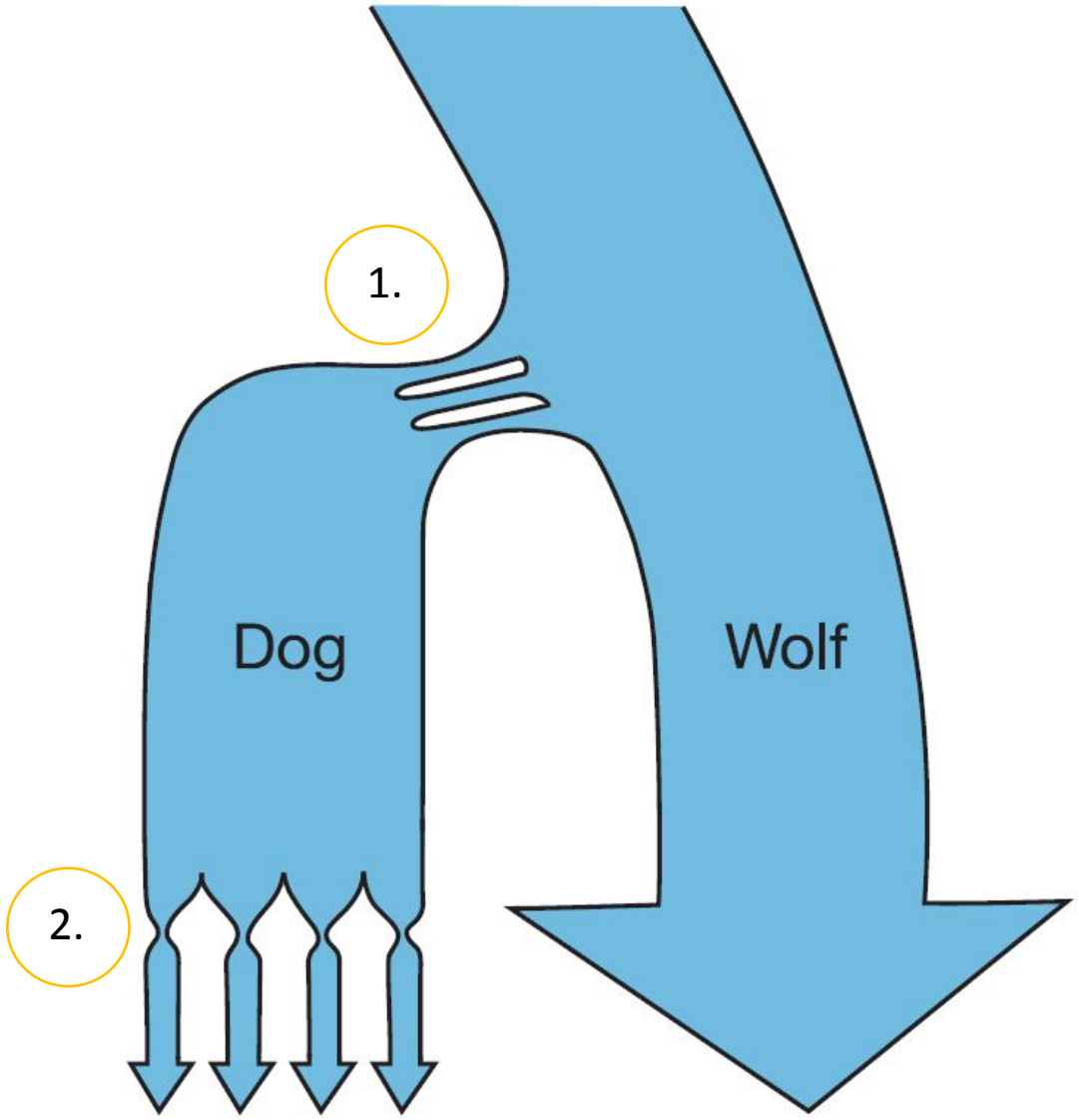
- Improved joints
- Better suited behaviourally
- **Focus on genetic diversity**

Why genetic diversity one of key features?

The cause of the high disease prevalence…

On the origin of the dog

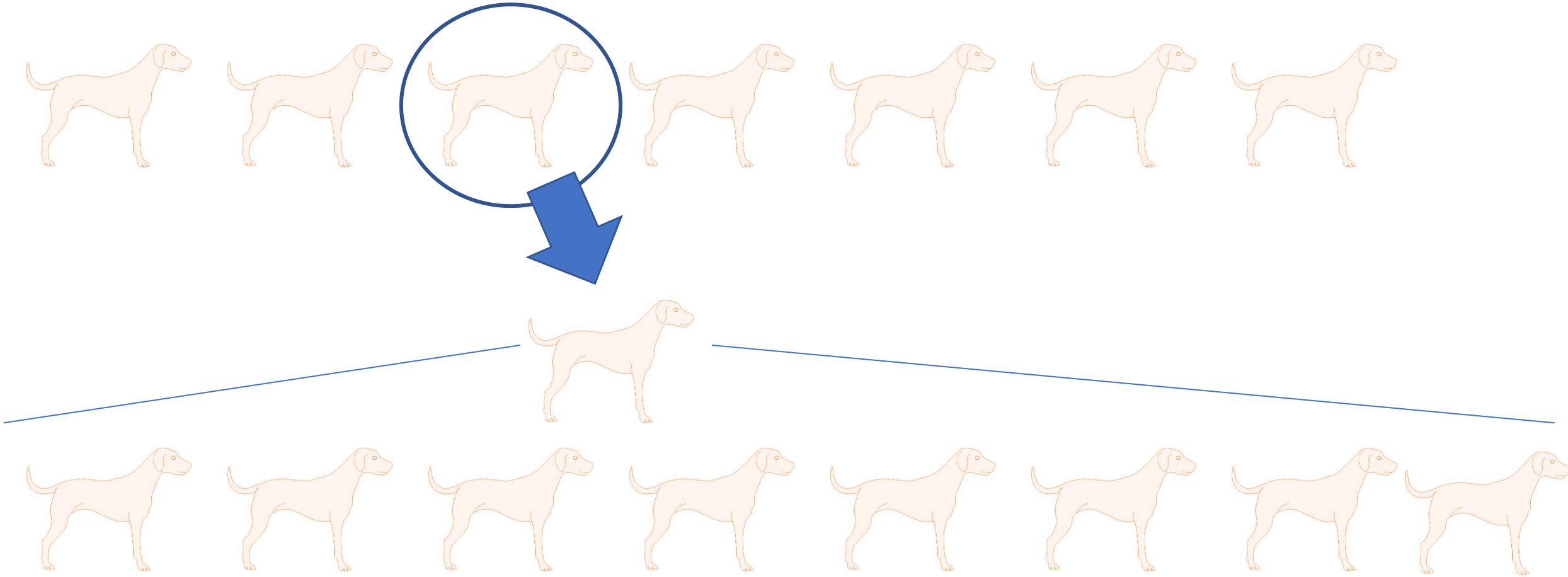
- Population “bottlenecks”
  1. Domestication
  2. Breed creation



Lindblad-Toh et al. (2005)

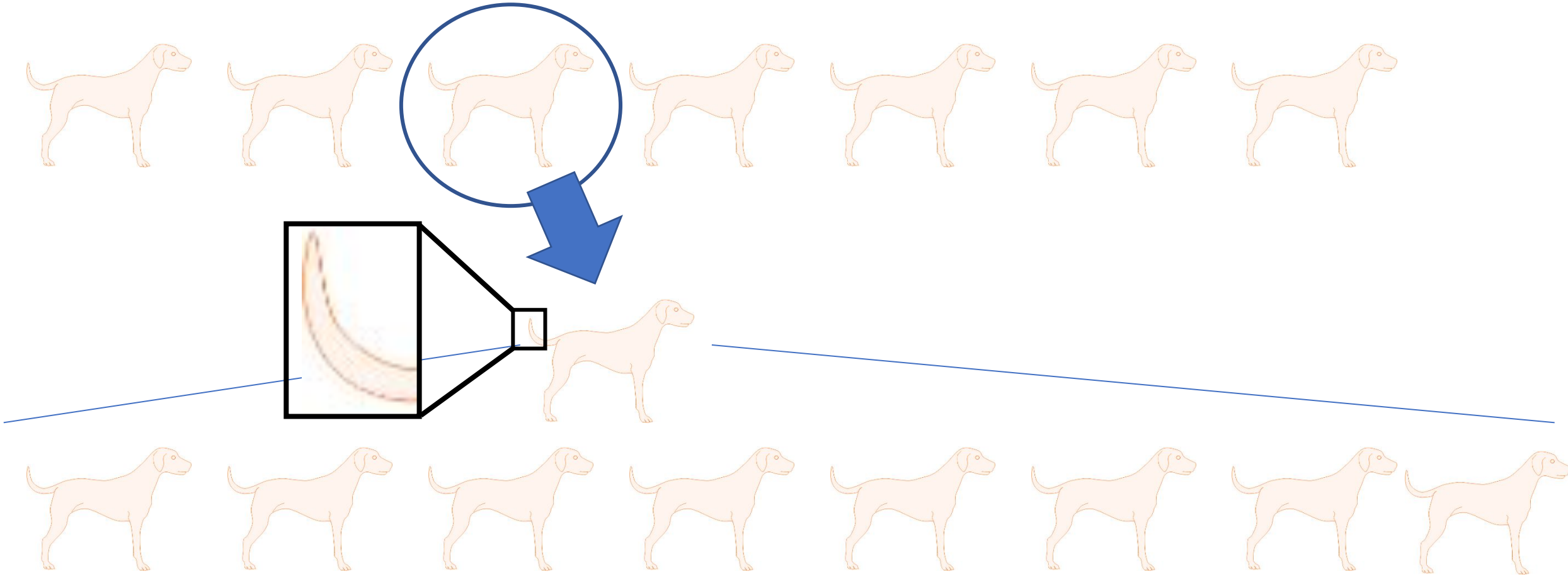
What are the consequences?

- At the level of the dog



What are the consequences?

- At the level of the dog



What are the consequences?

- At the level of the dog
- At the DNA level

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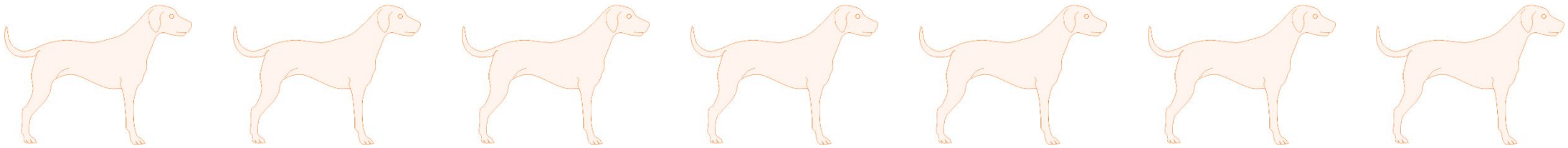
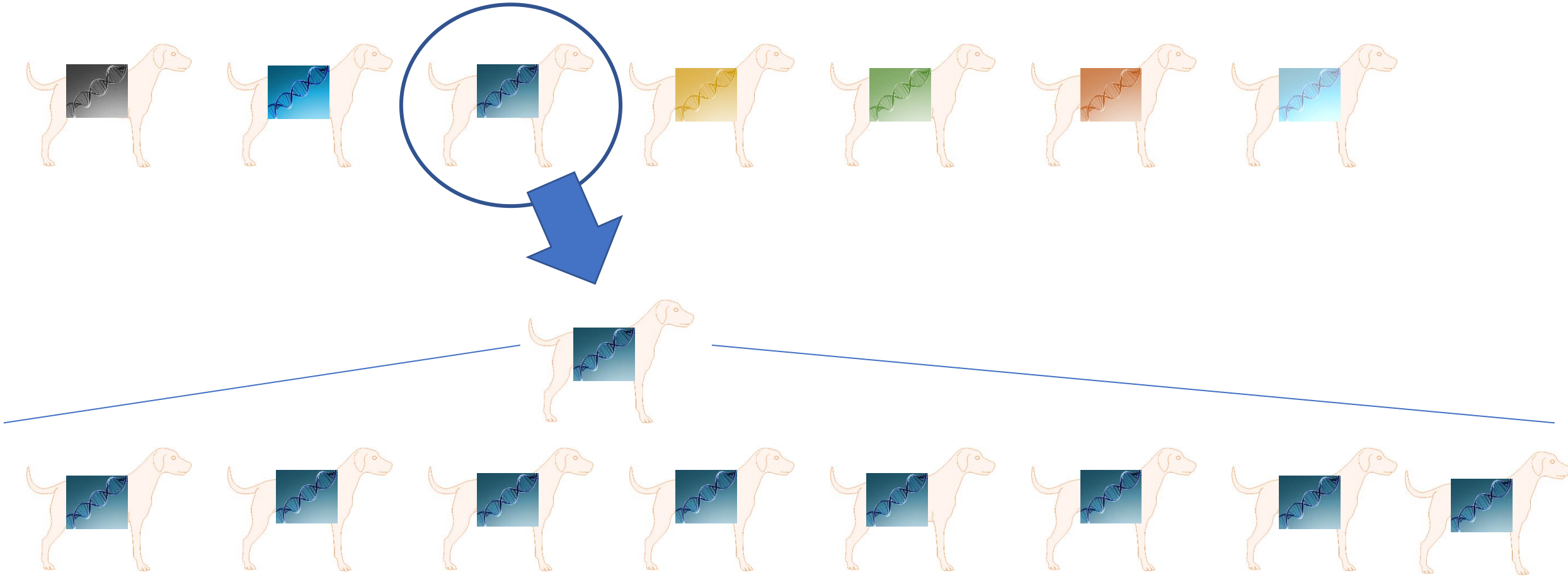
- At the DNA level



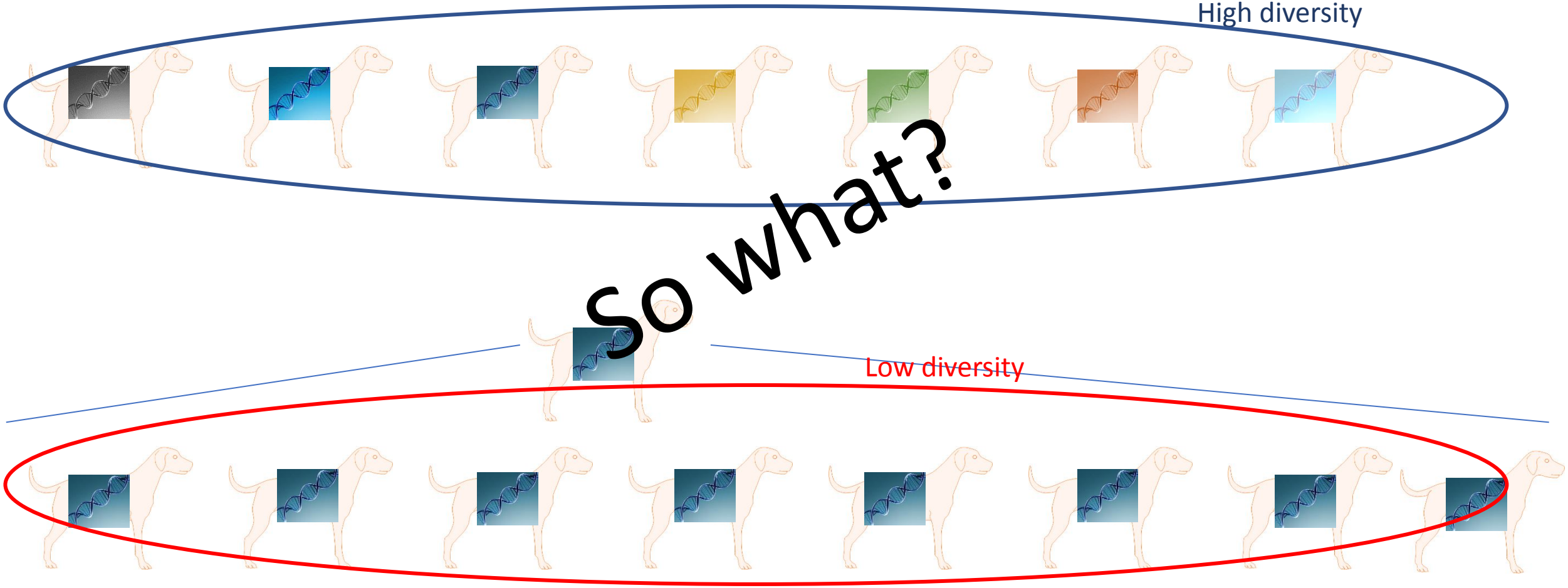
What are the consequences?

- At the DNA level



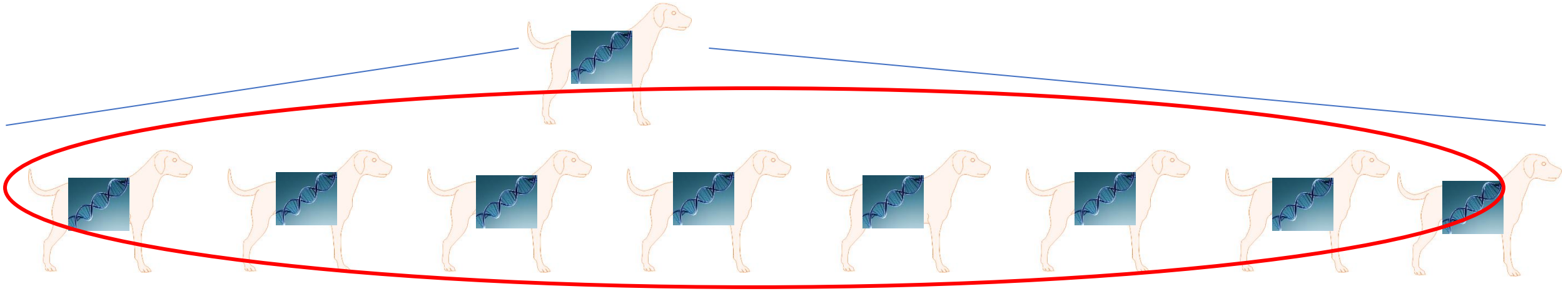
What are the consequences?

- At the DNA level



Every dog/human carries genetic diseases

- At the DNA level



⇒ Big part of the population carries the same mutation!

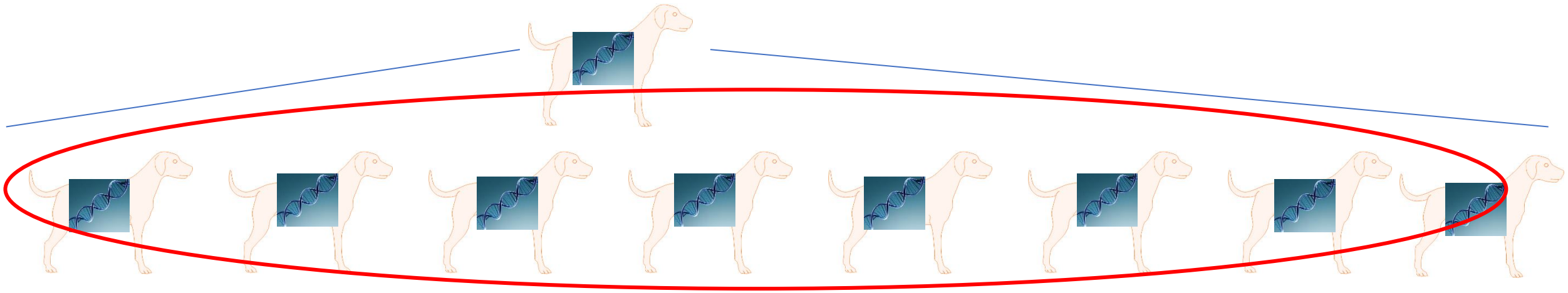
⇒ Population bottlenecks are responsible for the spreading of diseases

What has caused the high prevalence of these disorders?

- Other examples with a similar effect:
  - **The “founder effect”**
  - The “popular sire effect”

Founder effect

- E.g. a new breeding project: starts from a limited number of founding dogs



What has caused the high prevalence of these disorders?

- Other examples with a similar effect:
  - The “founder effect”
  - **The “popular sire effect”**

Popular sire effect

- The overuse of a certain breeder

⇒ This (male) animal contributes too much to the next generations

⇒ Spread of its disease-causing mutations

What has caused the high prevalence of these disorders?

- Other examples with a similar effect:
  - The “founder effect”
  - The “popular sire effect”

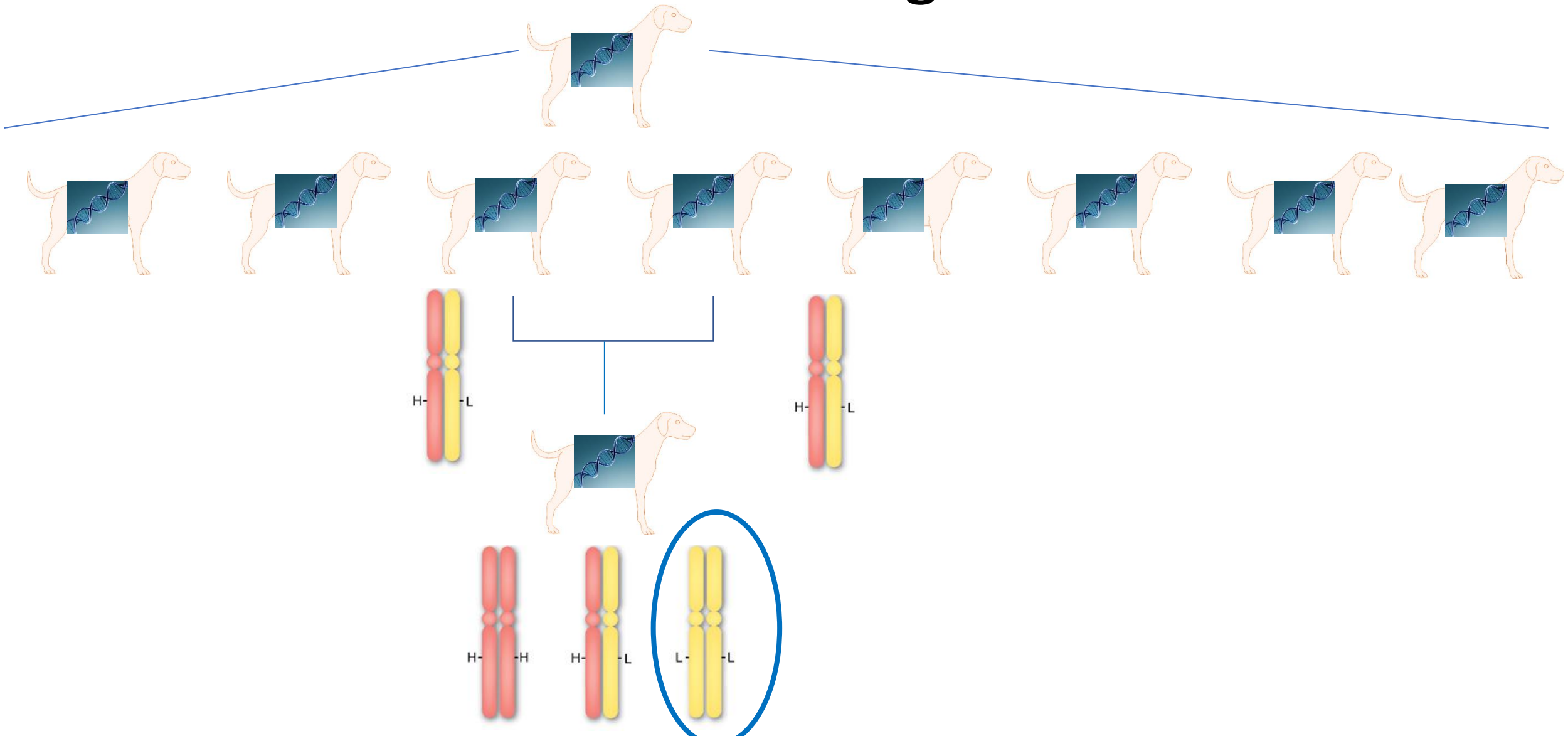
  ⇒ **The spread of disease-causing mutations**
- But what about inbreeding?

Inbreeding

- Definition:

*"The mating of two genetically related individuals is called **inbreeding**"*

Inbreeding



Inbreeding

- Definition:

*"The mating of two genetically related individuals is called **inbreeding**"*

- Diseases become visible

What has caused the high prevalence of these disorders?

- The combined effect of:
  - Bottlenecks
  - Founder effect
  - Popular sire effect
  - Inbreeding

What has caused the high prevalence of these disorders?

- The combined effect of:
  - Bottlenecks
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  - Popular sire effect
  - Inbreeding

Genetic diversity should ALWAYS be taken into account!

$\Rightarrow$ We have to learn from the past!

But how?

Practically

Size matters

Genetic diversity:

- Focus on N_e = effective population size

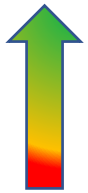
⇒ Based on how you manage your population, how many animals are there genetically present in your breeding program?

≠ the number of animals you have

Effective population size N_e

What is a good N_e?

- Cut-offs often reported:
  - N_e = 100
  - N_e = 50
  - N_e = 25



- Arbitrary, but the higher the better

Effective population size N_e

Various calculation methods:

- Link with number of bitches and studs:

$$N_e = \frac{4n♂n♀}{n♂ + n♀}$$

Practically: a population of 1000 dogs =>

1) one stud and 999 bitches Ne = 3.996

2) 500 studs and 500 bitches Ne = 1000

Effective population size N_e

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Advice 1: balance the number of bitches and studs

Effective population size N_e

Various calculation methods:

- Link with number of bitches and studs:

$$N_e = \frac{4n♂n♀}{n♂ + n♀}$$

Advice 1: balance the number of bitches and **studs**

Semen collection and continue training:

⇒ No loss of time invested by trainers

⇒ No loss of valuable genetic material

Effective population size N_e

Various calculation methods:

- Link with number of bitches and studs:

$$N_e = \frac{4n♂n♀}{n♂ + n♀}$$

Practically: size of the breeding program =>

1) 10 bitches and 10 studs $N_e = 20$

2) 20 bitches and 20 studs $N_e = 40$

Effective population size N_e

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Practically: size of the breeding program =>

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Effective population size N_e

Various calculation methods:

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$$N_e = \frac{4n♂n♀}{n♂ + n♀}$$

Advice 1: balance the number of bitches and studs

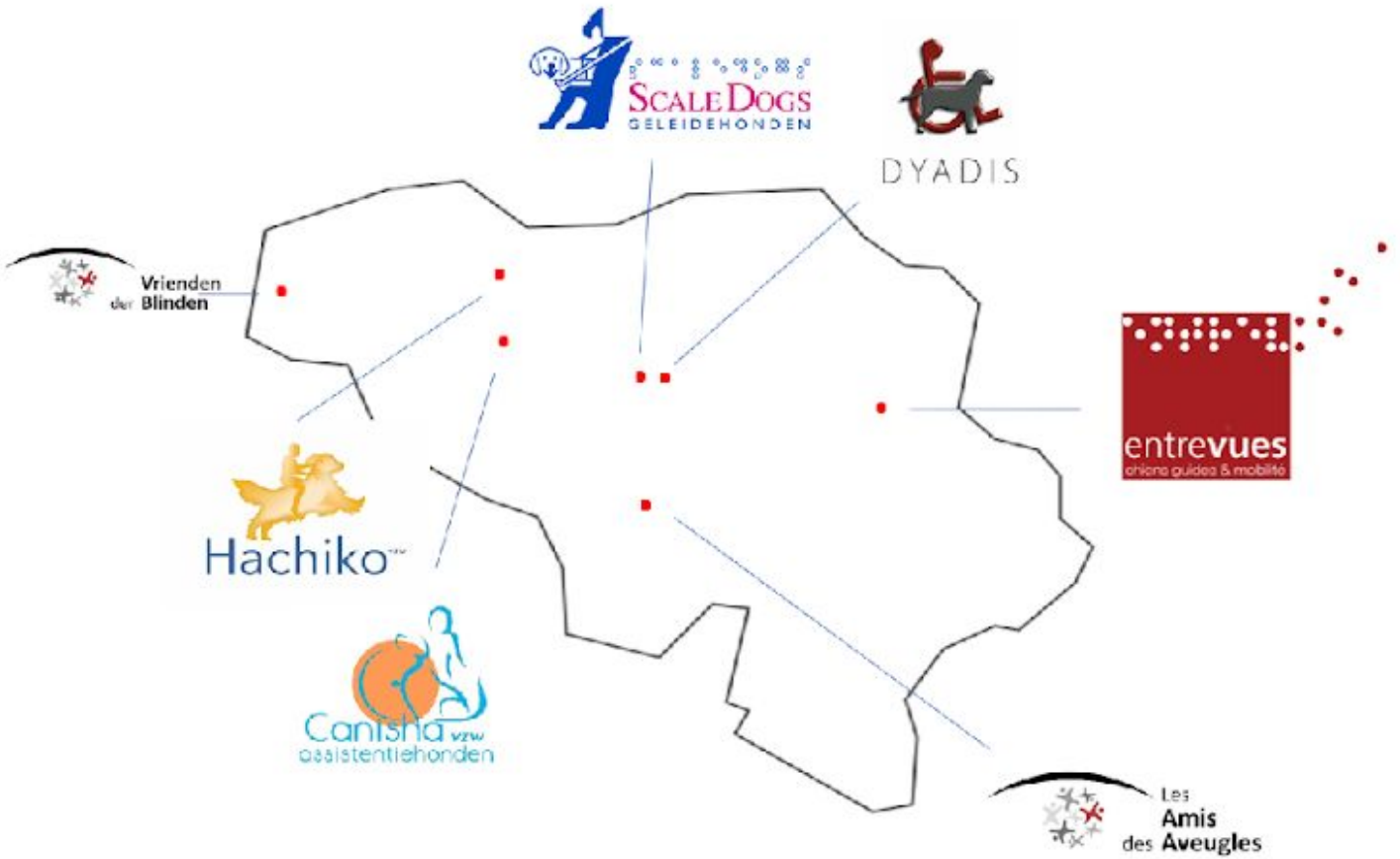
Advice 2: increase the size of the breeding program

Purpose Dogs

- Breeding project for 1 association

Purpose Dogs

- Breeding project for 1 association => Breeding project on a national scale



Effective population size N_e

Various calculation methods:

- Link with number of bitches and studs:
- Link with inbreeding coefficient (F or COI):

$$N_e = \frac{1}{2\Delta F}$$

What is ΔF?

The **increase** of the coefficient of inbreeding

Calculation of coefficient of inbreeding

- Search for common ancestor(s)

Practically:

- # Ancestors = 2^n with *n* the number of generations

e.g. 2 parents => 4 grandparents => 8 great-grandparents => 16 … => 32 … => 10^{th} generation: 1024 => 15^{th} generation: > 30 000

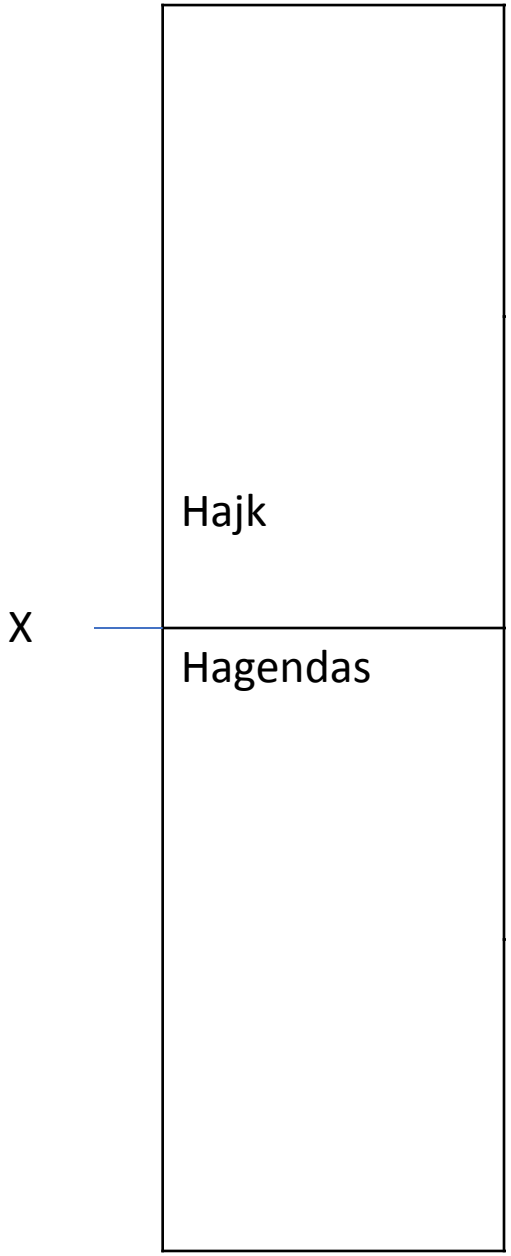
⇒ Finding a common ancestor ≠ horrible

⇒ What is important: is the **amount** of inbreeding/**magnitude** of the inbreeding coefficient

coefficient of inbreeding

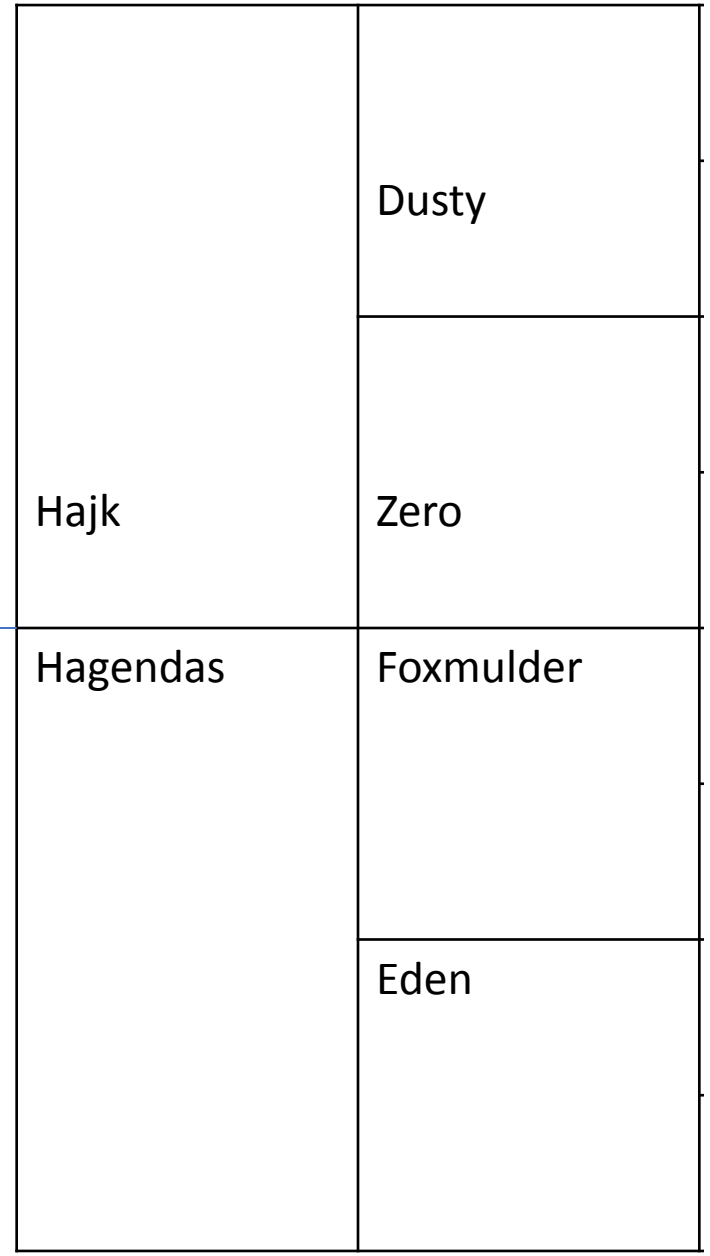
- Pedigree completeness = key

COI = 0



COI = 0

X



COI = 0 => 0.03

X

Hajk	Dusty	Phil
		O'Joint
	Zero	Snuffy
		Vecheyenne
Hagendas	Foxmulder	Dust
		Belle
	Eden	Shadow
		Vecheyenne

COI = 0 => 0.03 => …

X

Hajk	Dusty	Phil	Tennessee
			Brandy
		O'Joint	Jolt
			Elvira
	Zero	Snuffy	Scotch
			Caledonia
		Vecheyenne	Snickers
			Quoia
Hagendas	Foxmulder	Dust	Dusty
			Vecheyenne
		Belle	Timon
			Vecheyenne
	Eden	Shadow	Timon
			Ruby
		Vecheyenne	Snickers
			Quoia

Snickers

…

COI = 0 => 0.03 => **0.1956**

X

Hajk	Dusty	Phil	Tennessee	
			Brandy	
		O'Joint	Jolt	
			Elvira	
	Zero	Snuffy	Scotch	Snickers
			Caledonia	
		Vecheyenne	Snickers	
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Hagendas	Foxmulder	Dust	Dusty	…
			Vecheyenne	
		Belle	Timon	
			Vecheyenne	
	Eden	Shadow	Timon	
			Ruby	
		Vecheyenne	Snickers	
			Quoia	

coefficient of inbreeding

- Pedigree completeness = key
- Increase in number of ancestors known:
  - More correct estimates!
  - Calculation becomes more difficult

⇒ Use software

Effective population size N_e

Various calculation methods:

- Link with number of bitches and studs:
- Link with inbreeding coefficient

$$N_e = \frac{1}{2\Delta F}$$

Advice 3: if several mating partners: choose the one which results in the lowest inbreeding coefficient for the progeny

Effective population size N_e

Various calculation methods:

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Advice 3: if several mating partners: choose the one which results in the lowest inbreeding coefficient for the progeny

Advice 4: limit the number of times one sire is used

Effective population size N_e

Various calculation methods:

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$$N_e = \frac{1}{2\Delta F}$$

Advice 3: if several mating partners: choose the one which results in the lowest inbreeding coefficient for the progeny

Advice 4: limit the number of times one sire is used

Advice 5: international collaboration

International collaboration

- Pro:

"new" genetic material => genetic diversity ↗

- Con:

Potentially unpredictable results

⇒ Check whether you have the same screening tools/standards/…

Balance input!

Results

Results

- Diversity:
  - 4 bitches
  - 4 studs

$N_e = 8$

Results

- Diversity:
  - 4 bitches => 11 bitches
  - 4 studs => 10 studs
  - N_e (based on ΔF) =

$N_e = 8 \Rightarrow N_e \approx 21$

- Succes%:

Not bred by Purpose Dogs:	38 – 50%
Bred by Purpose Dogs:	63 – 71%

Overall: + 21%

Conclusion

- **The** cause of widespread genetic diseases
- Not necessarily easy to understand/nor calculate
- Essential to take into account
- Improved phenotypes AND high diversity => both possible!

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PADS

Genetic Diversity Put Into Practice

With the science in mind, how do we ensure we have enough genetic diversity?

PADS

Breeding program since 2001

Challenges:

How to prioritize diversity?

- Geographically isolated
- Most assistance dog schools small, limited cooperation

Advantages:

- Seeded with puppies & stud services by established schools
- Formation of ABC
- Trust of our Training department & management

PADS

Current Composition:

- Female breeders: 17
- Male breeders: 5
- Use of outside males/yr: avg 6

Breeder Selection Targets/Yr:

- Females: 6
- Males: 1-2

Approaches to Diversity – Stock Acquisition

- Not assistance/guide dog bred
  - Traits looking for?
  - Consistency?
  - More readily available
  - Risk of less success
  - Turning over generations quickly
  - What you breed them to
- Purpose assistance/guide dog bred
  - Traits looking for
  - Consistency
  - Less readily available
  - Odds of greater success

Diversity not just about #’s – need quality

Approaches to Diversity – Access to More (Quality) Stock

- Puppy acquisitions
- Stud services (fresh, frozen)
- Multisire litters
- Partnerships with individual schools
- Cooperatives
- Commercial breeders of guide/assistance type pups

Cooperatives: International Breeding Cooperative (IBC)

- 68 member organizations across 3 regions/continents, 9 countries
- Large breeding population housed across Host member schools
- Increased access to quality diverse stock
- Common measurements & data storage platform

Approaches to Diversity – What To Keep/Cut

Produce & Keep More Breeders

- Few litters = few replacement breeders.
- Few breeders = less diversity

Effective population size N_e

Various calculation methods:

- Link with number of bitches and studs:

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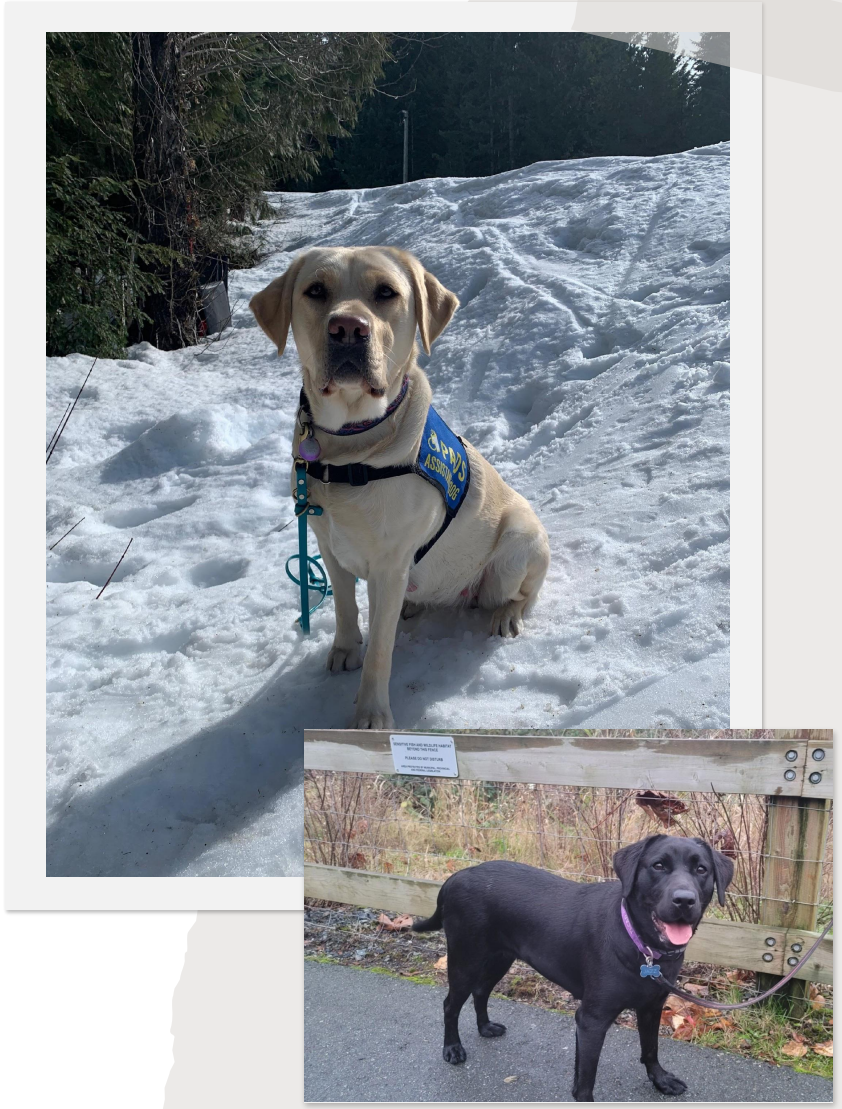
Practically: size of the breeding program =>

1) 10 bitches and 10 studs $N_e = 20$ ✘
2) 20 bitches and 20 studs $N_e = 40$ ✓

Options to Increase Diversity - Females

- Breed each female fewer times over normal career timespan
- Breed per normal schedule, distribute excess
- Turn over generations quickly & return to training
- Loan/Exchange with other organizations



Options to Increase Diversity – Males

- Career studs
- Short term studs or
- Freeze & neuter
- Other schools' studs
- Stud Services to other schools

Semen Banking – Scenarios & Considerations

Training needs good dogs

Advantages of banking semen and returning to training:

- Balances diversity & placement needs
  - Top males can be used for both breeding & placed with a client
  - More studs from one litter can be used without impacting Training's production – increases diversity (# genes for each parent represented)
  - Limits your use of stud
- Diversity "insurance" to fall back on
- Impacts on placement success/behaviour?

Semen Banking – Other Impacts on Diversity

- Ability to freeze semen for later use on short-term exchange studs
- Ability to assess production & use stud further
- Acquiring semen from proven studs with EBVs from other schools
- Options for hard-to-pair females (low genetic diversity, Carrier statuses or EBVs, shipping disruptions) – dip into the tank
- Bring back lost diversity

Barriers to Diversity

- Borders
  - Regulations
  - Quarantines
  - Physical barriers
- Shipping
  - Shipping companies
  - Customs
  - Holidays
- Disruptions
  - COVID
  - Civil conflict / War
  - Weather

Further reasons to have frozen semen, partnerships with other local schools

Tradeoffs to Diversity

- Bringing in new stock, potential for less consistency in early generations – different selection criteria & preferences between organizations
- Potential to introduce new “problem” genes, but at lower frequency

Thank you!

Jackie Clark
Breeding and Puppy-Raising Manager
Pacific Assistance Dogs Society (PADS)

E-mail: jackie@pads.ca