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The impact of genomic selection on genetic diversity and genetic gain in French dairy cattle breeds

Anna-Charlotte Doublet[1,2], Pascal Croiseau[1], Sébastien Fritz[1,2], Chris Hozé[1,2],
Alexis Michenet[1,2], Denis Laloë[1], Gwendal Restoux[1]

[1] GABI, INRA, AgroParisTech, Université Paris-Saclay, 78350 Jouy-en-Josas, France
[2] ALLICE, Paris, France

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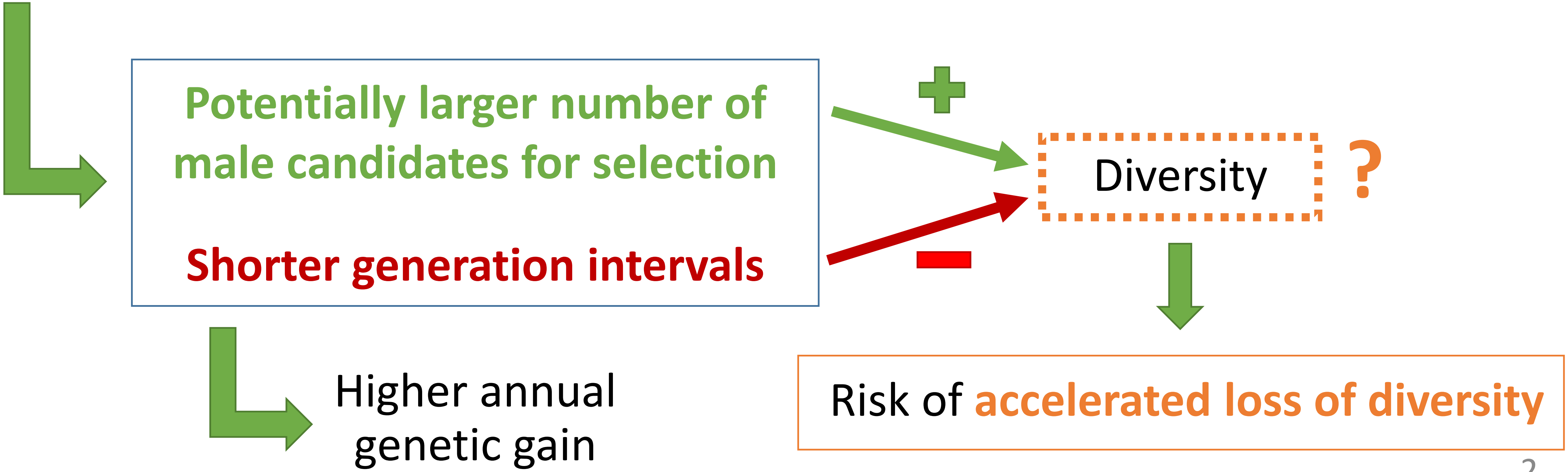
Context – From genetic to genomic selection in dairy cattle in France

Genomic selection in dairy cattle breeds ⇒ **New breeding schemes**

Before 2010: Genetic selection	**2010-2012: Transition phase**	**Since 2012: Genomic selection**
Progeny testing Sires of bulls ≈ 6 yo Dams of bulls ≈ 3 yo in farms	Intermediate situation	Genomic evaluation Sires of bulls ≈ 2 yo Dams of bulls ≈ 2 yo in donor stations



Potentially larger number of male candidates for selection

Shorter generation intervals

Higher annual genetic gain

Diversity

Risk of **accelerated loss of diversity**

Consequences of a loss of genetic diversity

Loss of additive genetic variance → **Loss of potential genetic gain**

Loss of overall genetic diversity → **Loss of adaptive potential**

Inbreeding depression → **Detrimental effects on fitness traits**

➔ **Economic impact**

Material

Marketed sires, genotyped in France from 3 French dairy cattle breeds

Montbéliarde
National breed


CC groms78

Normande
National breed

Holstein
International breed

Evolution of genetic diversity

Pedigree data:
Inbreeding

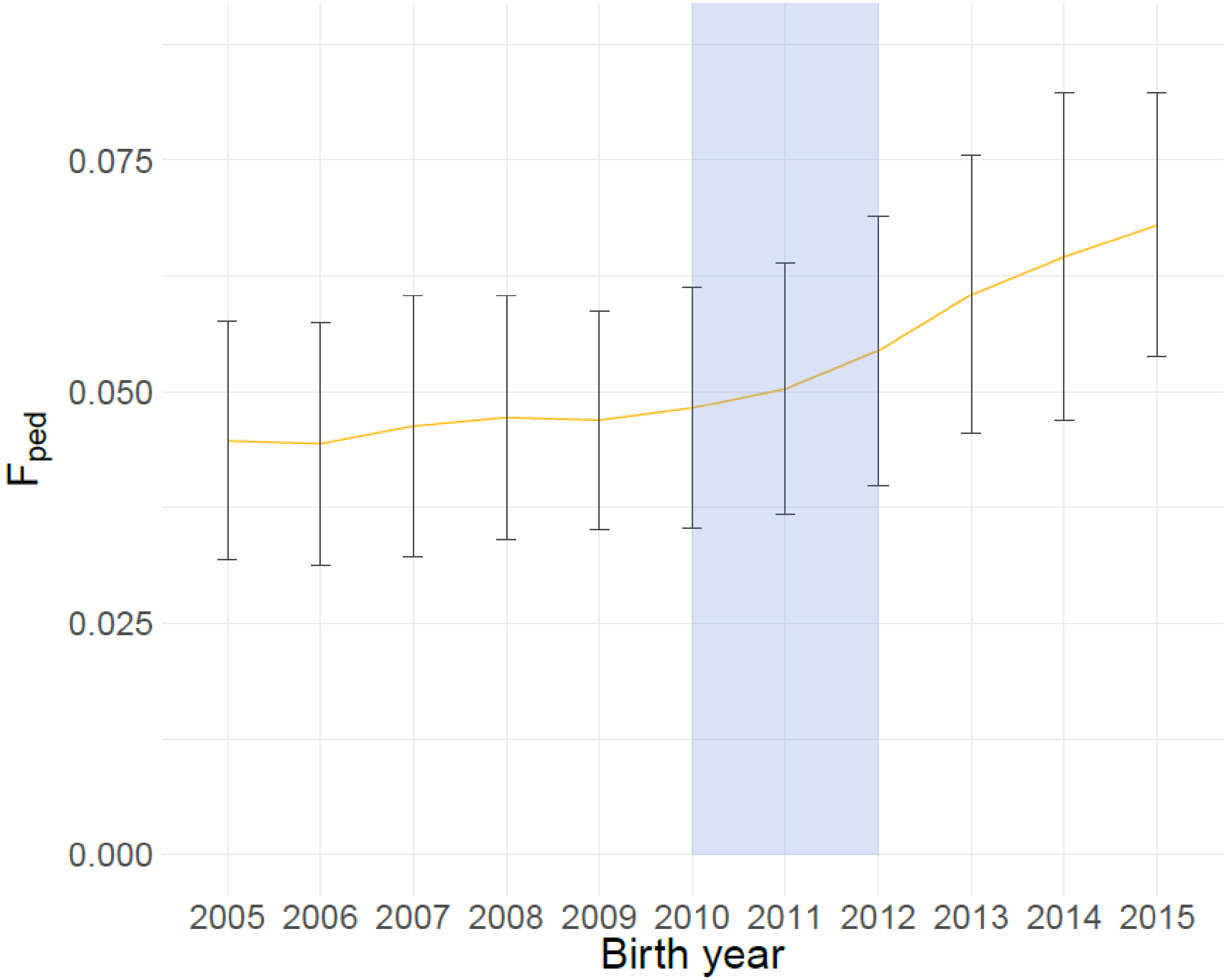
50K genotyping data (Runs Of Homozygosity):
Inbreeding
ROH length

Evolution of genetic gain

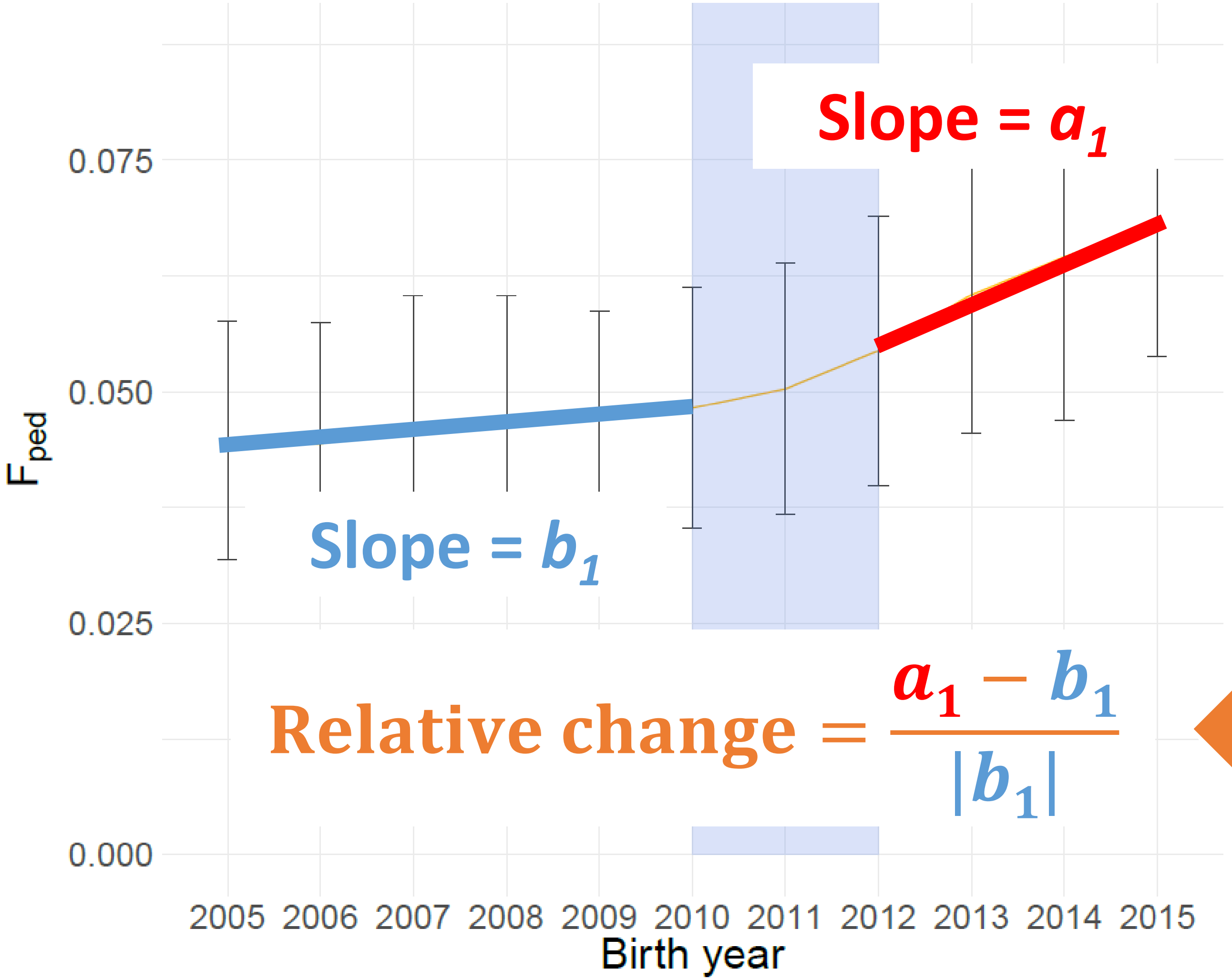
Total Merit Index

Combining production traits, functional traits and type traits

Display of results



Display of results



$$\text{Relative change} = \frac{a_1 - b_1}{|b_1|}$$

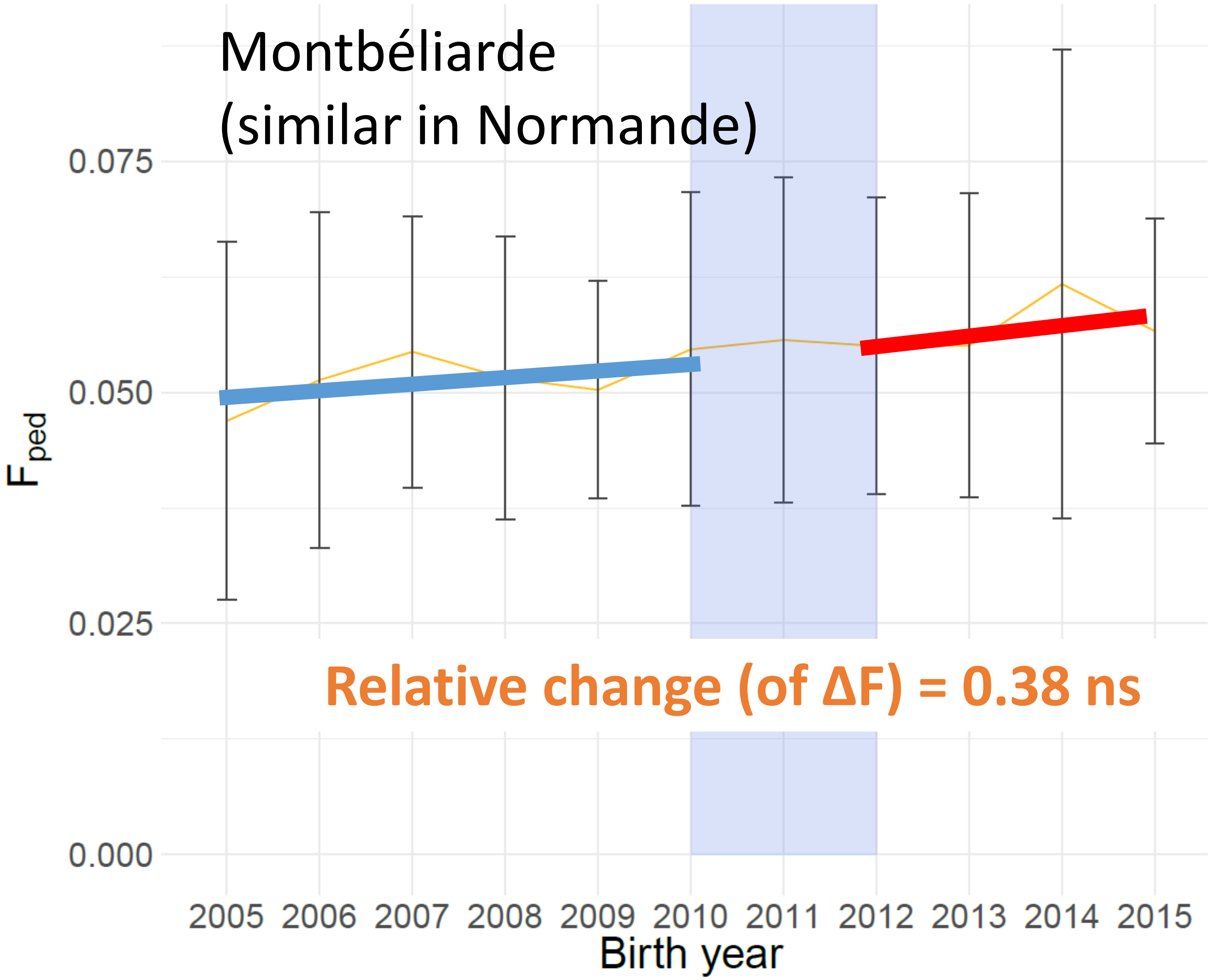
Comparison of the slopes
of each parameter **before** and **after**
the beginning of genomic selection

> 0 : acceleration
< 0 : deceleration

p-value: pairwise comparison of the slopes

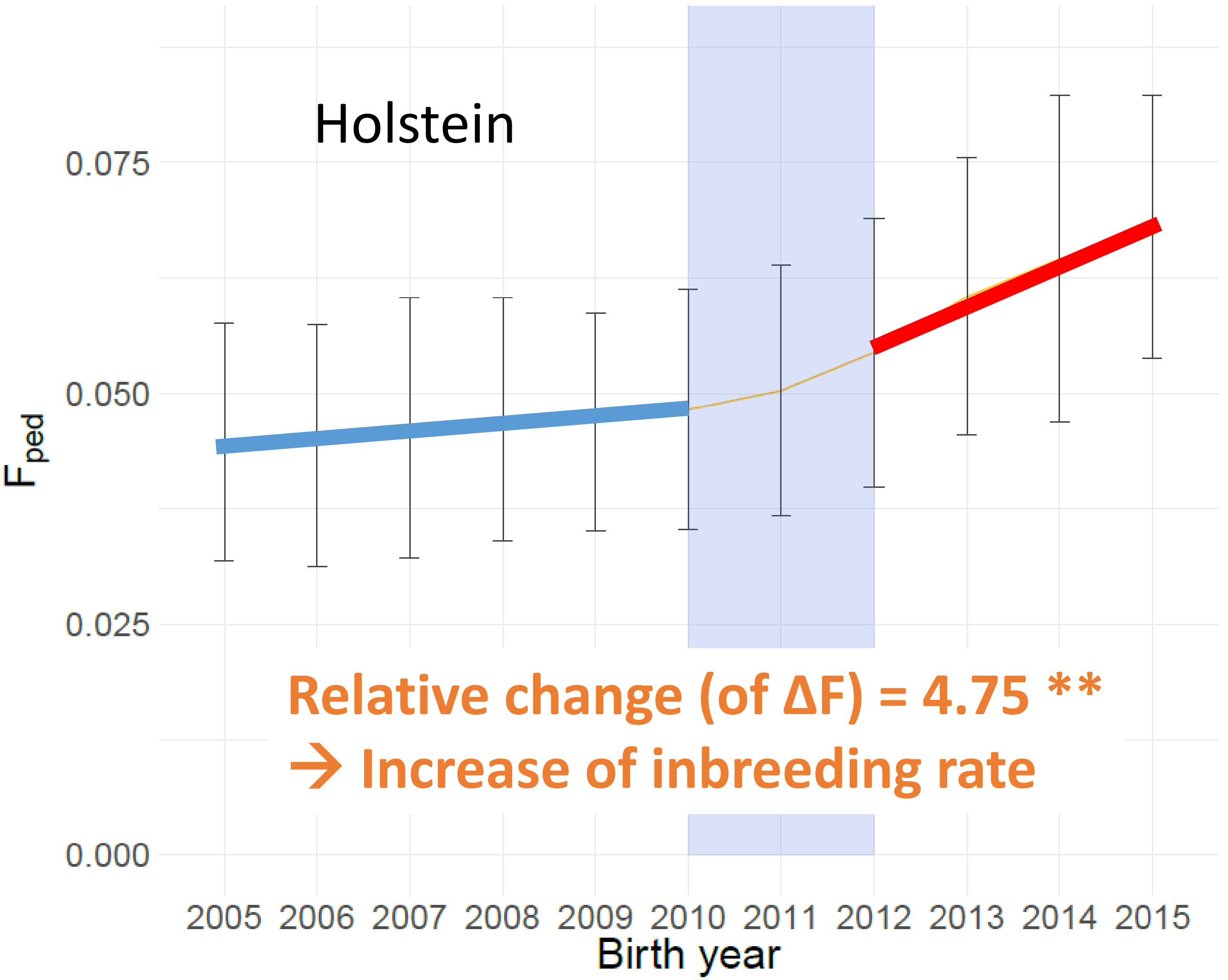
Inbreeding based on pedigree data F_{ped}

** p-value < 0.001
* 0.001 < p-value < 0.05
ns p-value > 0.05



Montbéliarde
(similar in Normande)

Relative change (of ΔF) = 0.38 ns



Holstein

Relative change (of ΔF) = 4.75 **

→ Increase of inbreeding rate

Runs Of Homozygosity (ROH)

= long genomic segments consisting of consecutive homozygous SNPs

≈ autozygous segments of the genome (IBD)

$$F_{\text{ROH}} = \frac{\text{Total length of the ROH of an individual}}{\text{Total length of the genome covered by SNPs}}$$

McQuillan *et al*, 2008, adjusted as done by Doekes *et al*, 2018

Shorter ROHs = older autozygosity
Longer ROHs = more recent autozygosity

Detected with PLINK (with 50K genotyping data)
- Minimal length = 1Mb
- Minimal number of SNPs per ROH = 15 SNPs
- Sliding window = 15 SNPs
- Minimal SNP density: 1 SNP / 75 kb
- Maximum gap: 150 kb

Inbreeding based on ROH F_{ROH}

** p-value < 0.001
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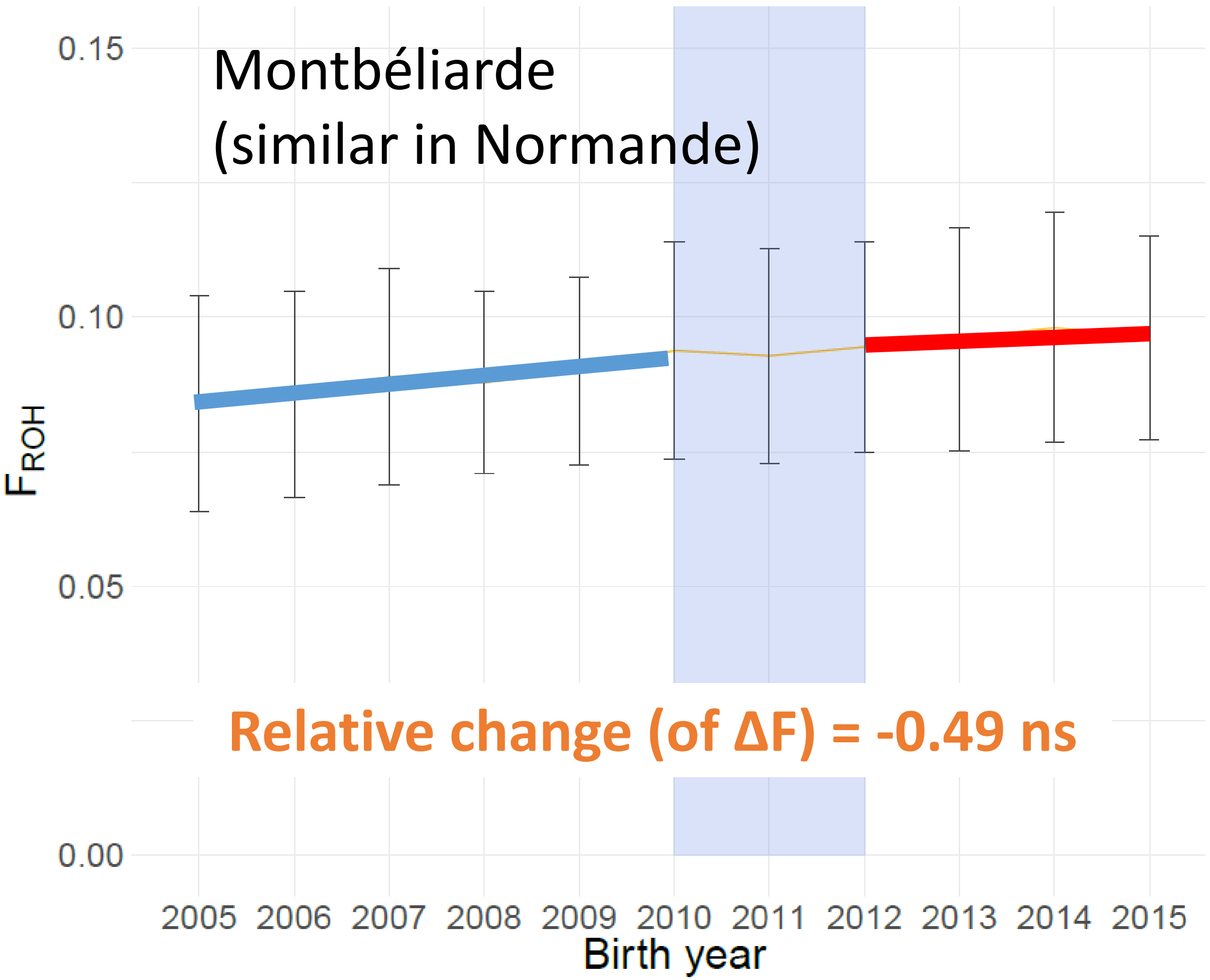
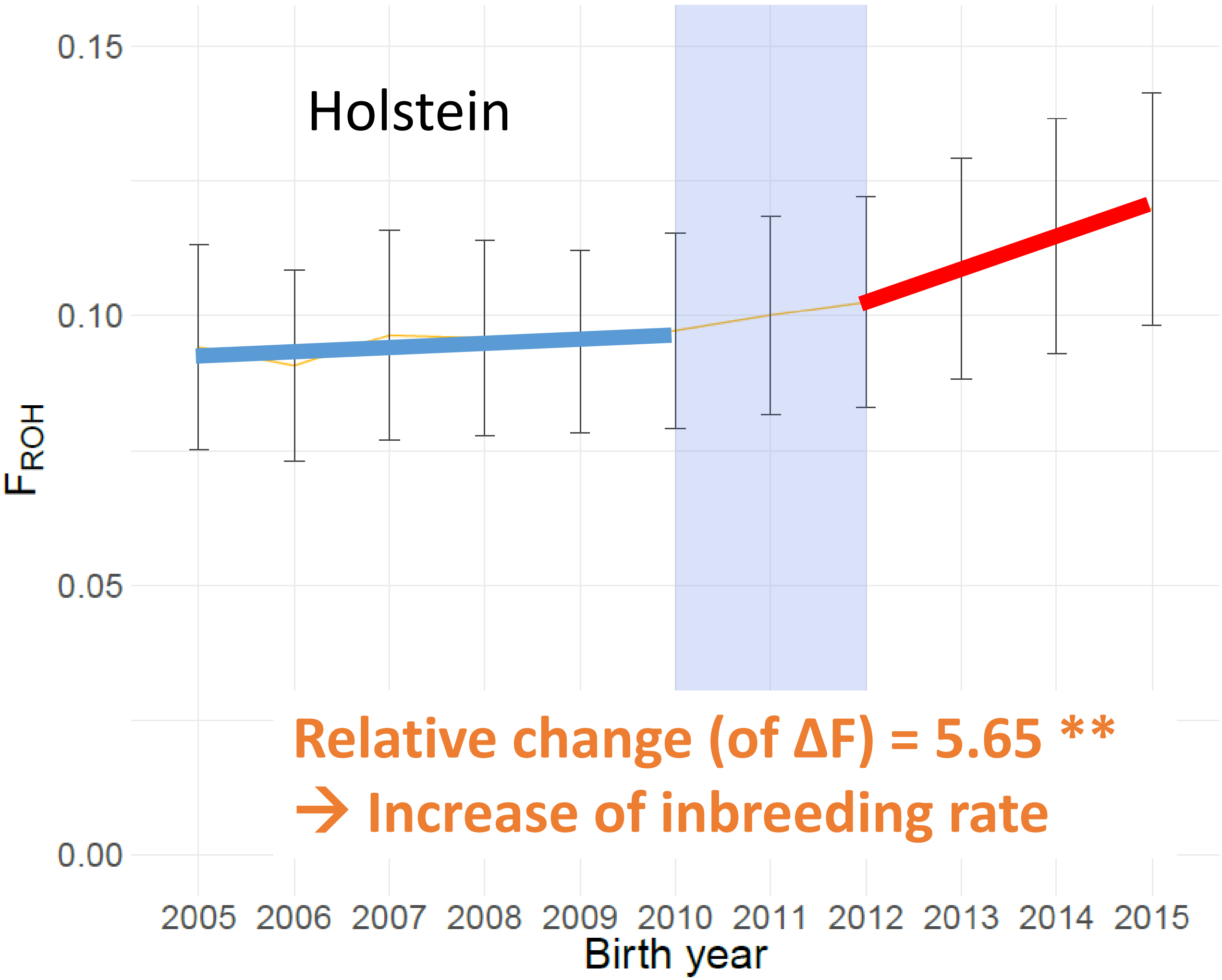
ns p-value > 0.05



Relative change (of ΔF) = -0.49 ns



Relative change (of ΔF) = 5.65 **
→ Increase of inbreeding rate

ROH length

** p-value < 0.001
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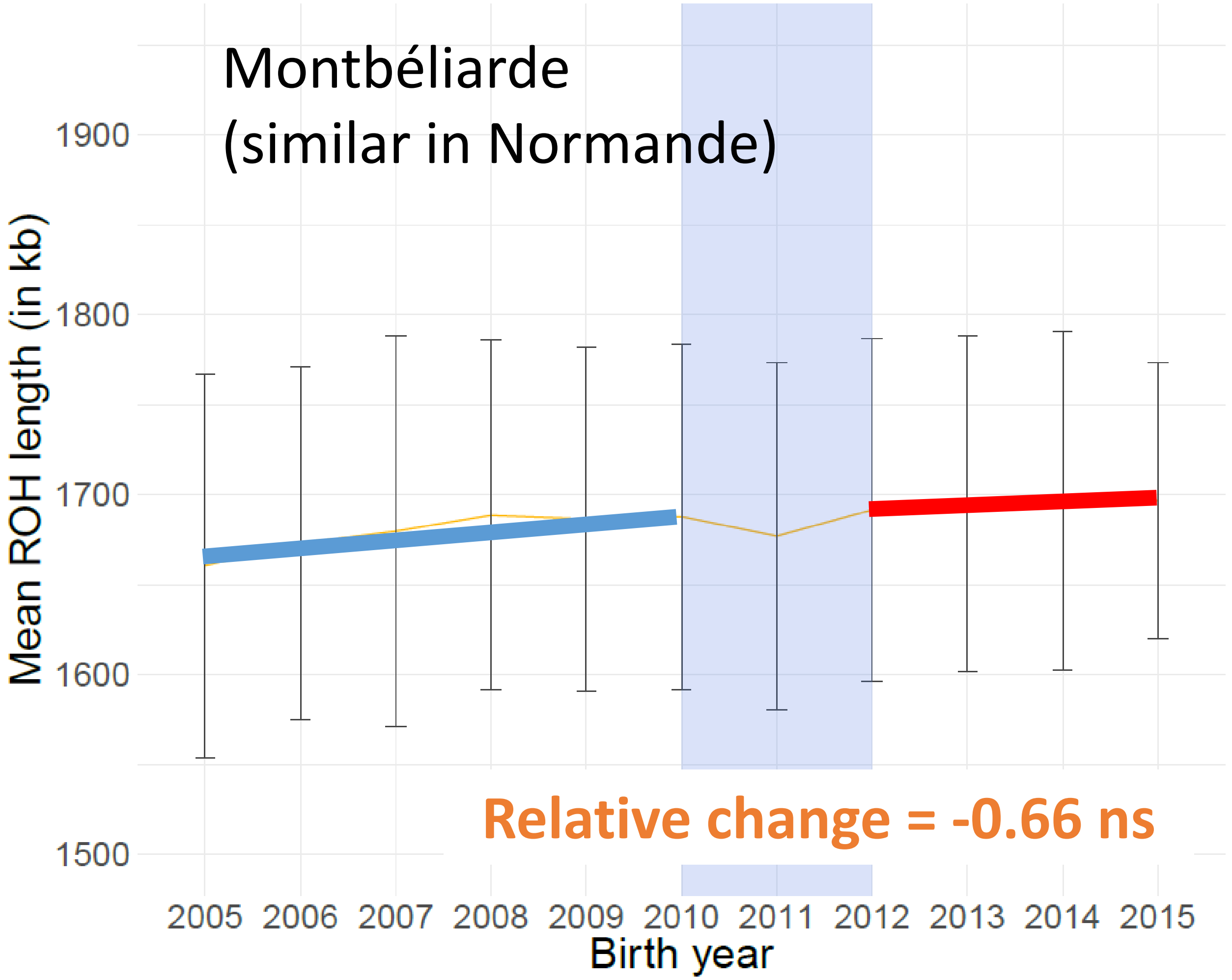
ns p-value > 0.05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(similar in Normande)

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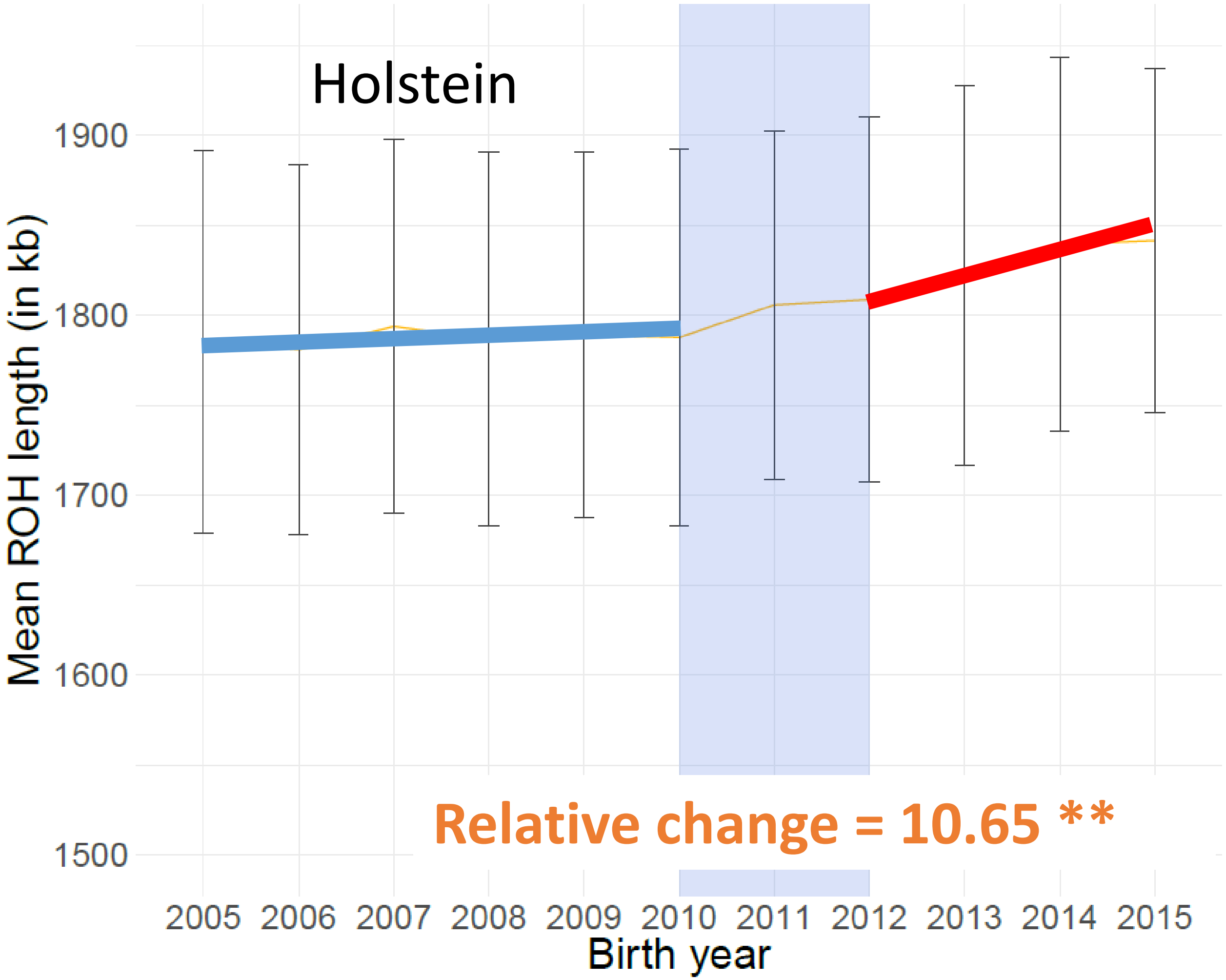
Holstein

Relative change = 10.65 **

Genetic gain TMI

** p-value < 0.001
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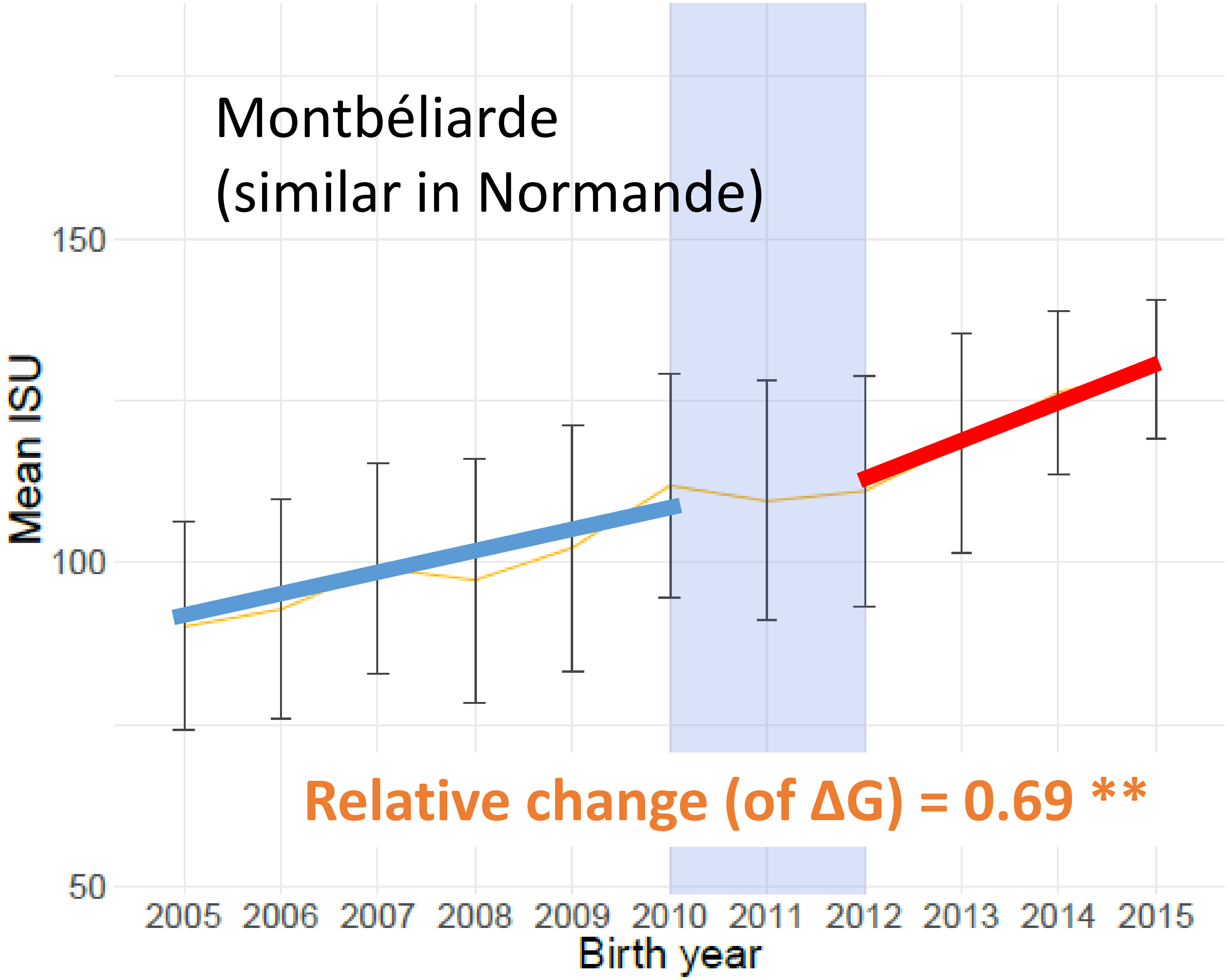
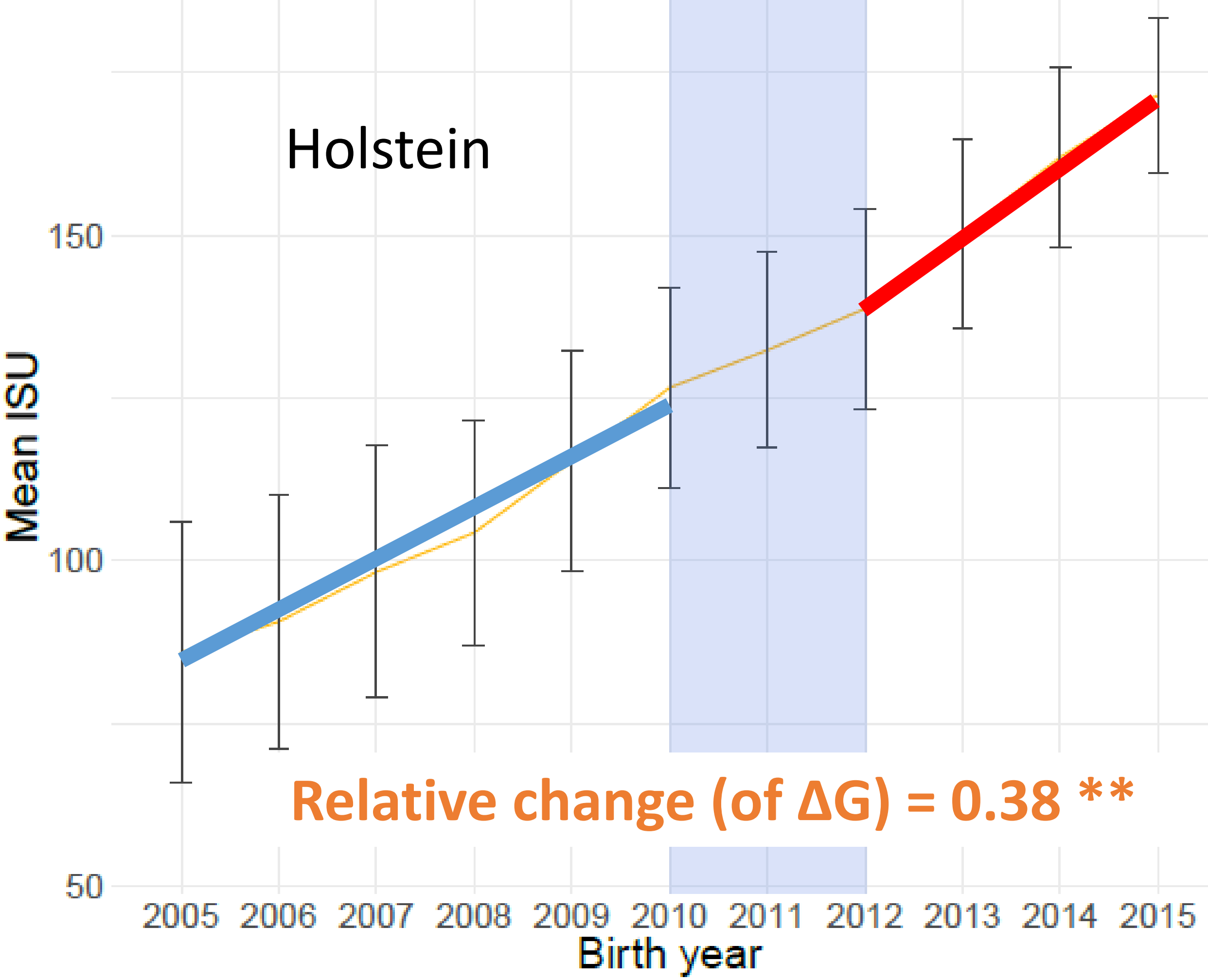
ns p-value > 0.05



Montbéliarde
(similar in Normande)

Relative change (of ΔG) = 0.69 **



Holstein

Relative change (of ΔG) = 0.38 **

Results – Impact of genomic selection

** p-value < 0.001
* 0.001 < p-value < 0.05
ns p-value > 0.05

$$\text{Relative changes} = \frac{a_1 - b_1}{|b_1|}$$

Breed	**Genetic gain** **TMI**	**Genetic diversity** F_{ped}	F_{ROH}	**ROH length**
Montbéliarde	**0.69 ****	0.38 ns	-0.49 ns	-0.66 ns
Normande	**0.71 ***	2.86 ns	-0.12 ns	-18.33 ns
Holstein	**0.38 ****	**4.75 ****	**5.65 ****	**10.65 ****

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Increased annual genetic gain for all breeds

Results – Impact of genomic selection

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Increase of the inbreeding rate in Holstein,
not in Montbéliarde and Normande
→ Results are consistent between pedigree and genomic data

Results – Impact of genomic selection

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Higher annual increase of the length of ROH in Holstein, not in Montbéliarde and Normande
→ Faster increase of recent inbreeding in Holstein

Discussion

In Holstein, in France: faster increase in recent inbreeding **+** accelerated loss of diversity

(Forutan *et al*, 2018; Doekes *et al*, 2018)

How to explain the difference between the 3 breeds?

1) Improved balance of the use of bulls in Montbéliarde and Normande but not in Holstein (already good before)

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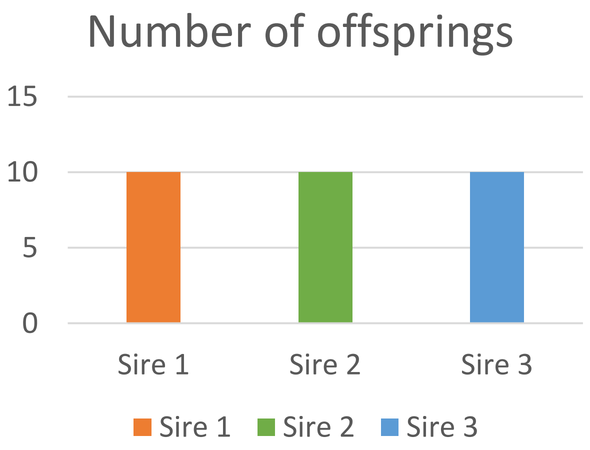
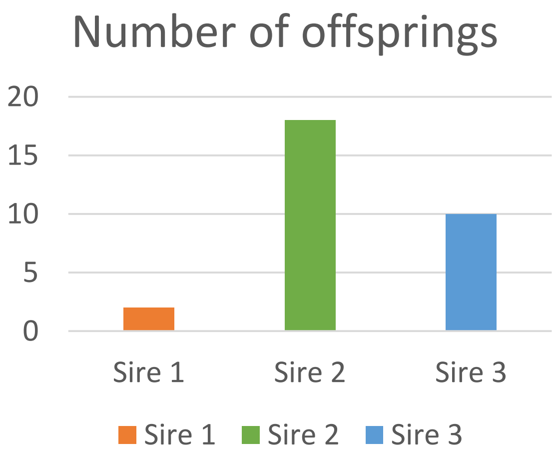
Sire use disequilibrium index:


Number of offsprings

Sire use disequilibrium index = 0


Number of offsprings

Sire use disequilibrium index > 0

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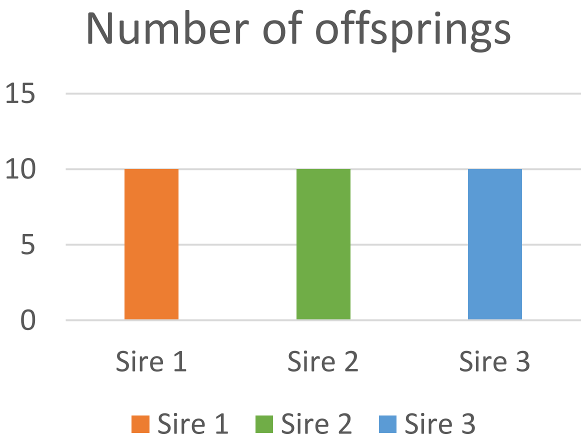
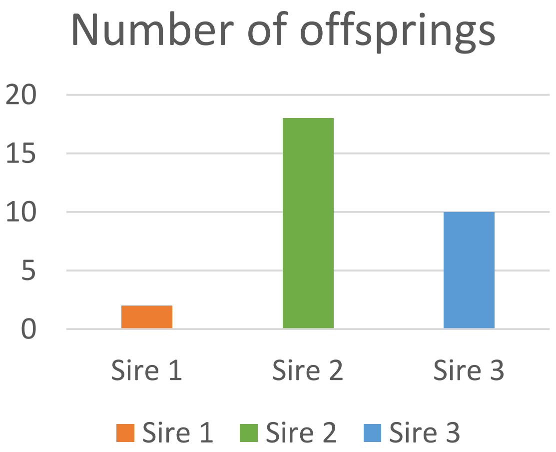
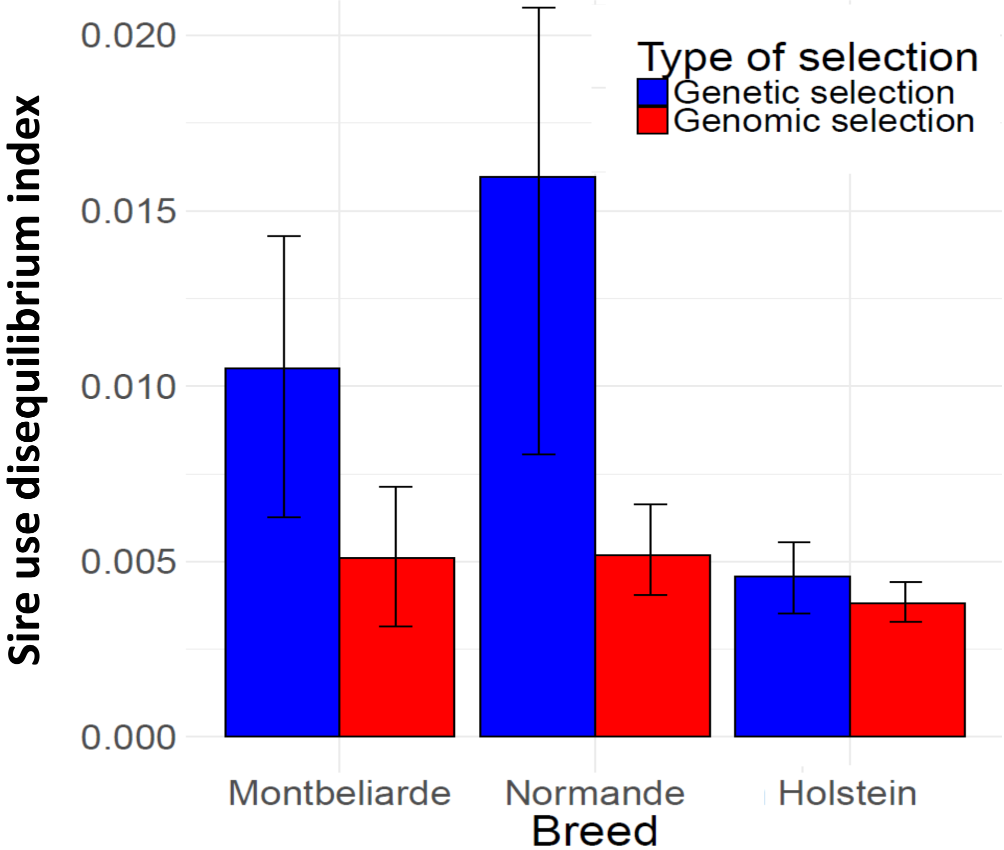


➡ **Sire use disequilibrium index = 0**



➡ **Sire use disequilibrium index > 0**



Discussion

In Holstein, in France: faster increase in recent inbreeding **+** accelerated loss of diversity
(Forutan *et al*, 2018; Doekes *et al*, 2018)

How to explain the difference between the 3 breeds?

1) Improved balance of the use of bulls in Montbéliarde and Normande but not in Holstein (already good before)

2) Higher increase in the effective number of sires in Montbéliarde and Normande (depending on their contribution to AI for a year):
    - Montbéliarde **x 3**
    - Normande **x 2.5**
    - Holstein **x 2**

Conclusion and perspectives

Genomic selection = new breeding schemes in France

In national breeds (Montbéliarde and Normande):
accelerated annual genetic gain without accelerated loss of genetic diversity

In international breed (Holstein): detrimental effect on genetic diversity

It could be the consequence of the way sires are selected and marketed
(turn over, proportion and number of semen doses per sire, etc.)

Perspectives:

Relevance of genomic measures of diversity
Analysis of the structure and repartition of ROHs
Impact of the use of foreign sires
Impact of national VS international breed management

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Perspectives:

Relevance of genomic measures of diversity
Analysis of the structure and repartition of ROHs
Impact of the use of foreign sires
Impact of national VS international breed management

Thanks

Allice

APIS-GENE

INRA GABI – PSGen and G2B teams

GDivSelGen project (SELGEN)

Thank you for your attention!

SUPPLEMENTARY SLIDES

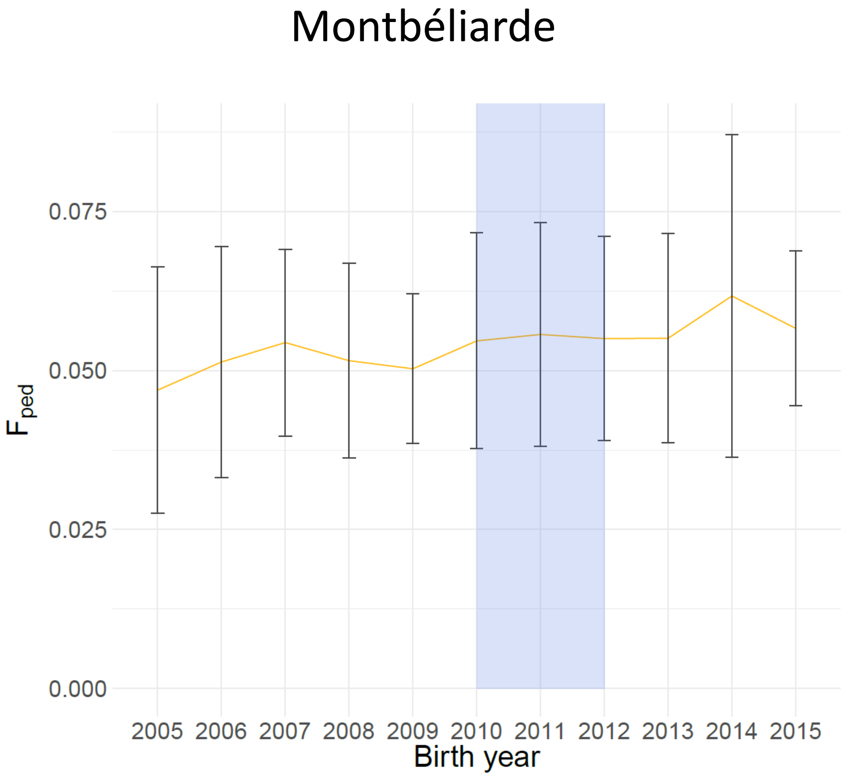
Number of animals and SNPs

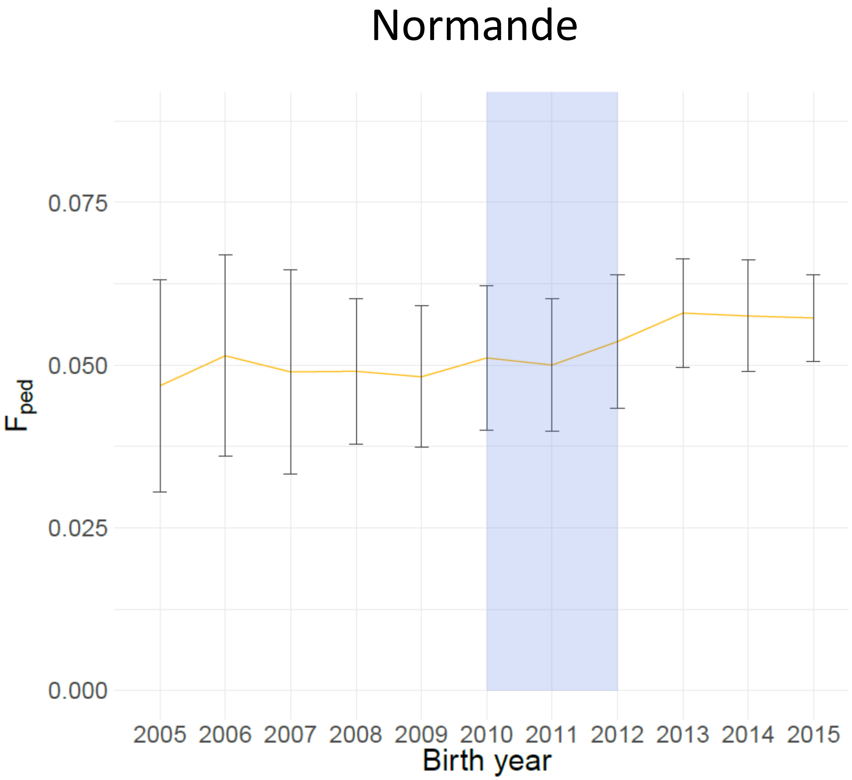
Breed	Number of animals born between 2005 and 2010	Number of animals born between 2012 and 2015	Number of SNPs
Montbéliarde	826	420	39,992
Normande	666	347	40,135
Holstein	3440	1248	41,377

F_{ped}

Breed	F_{ped}				
	b_1	Standard error	a_1	Standard error	Relative change
Montbéliarde	1.067E-03	3.423E-04	1.475E-03	7.901E-04	**0.382 ns**
Normande	2.991E-04	3.277E-04	1.153E-03	4.233E-04	**2.856 ns**
Holstein	7.783E-04	1.415E-04	4.472E-03	3.864E-04	**4.746 ****

F_{ped}


Montbéliarde
0.075
0.050
0.025
0.000
F_{ped}
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Birth year


Normande
0.075
0.050
0.025
0.000
F_{ped}
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
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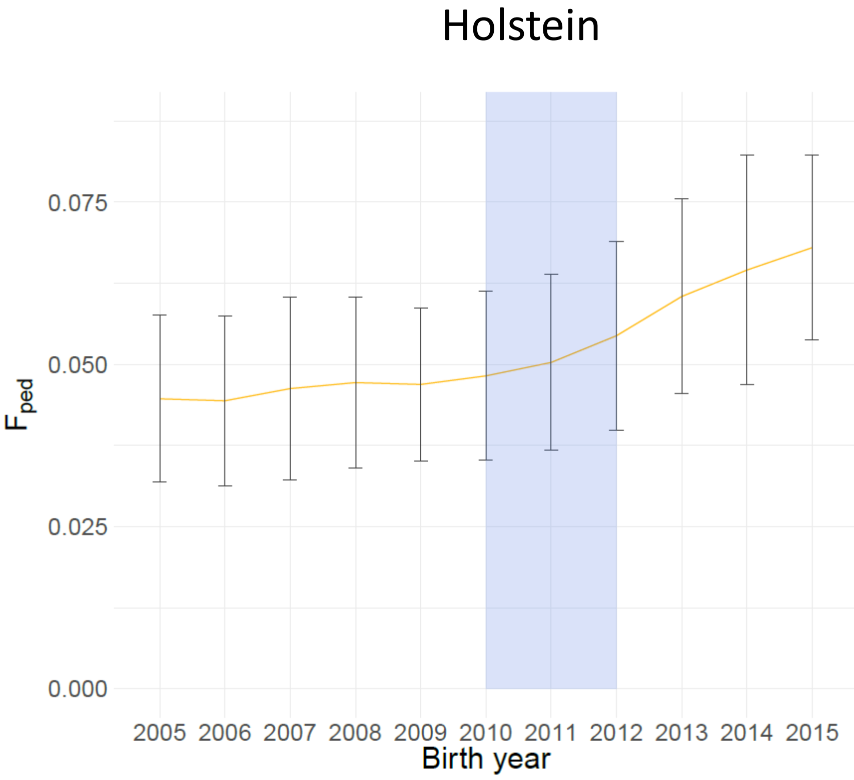

Holstein
0.075
0.050
0.025
0.000
F_{ped}
2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Birth year

Genome length

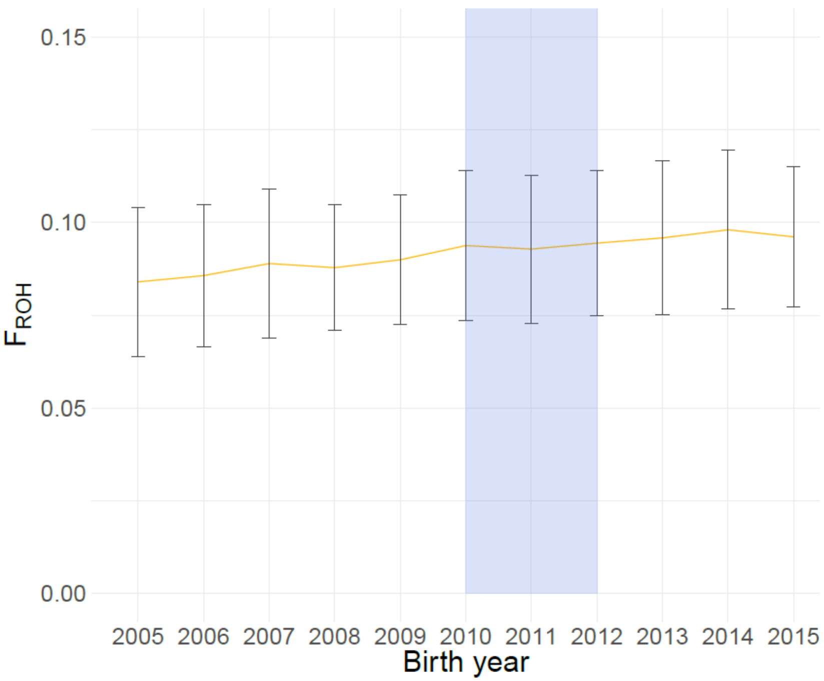
Breed	Length of genome covered by SNPs	Length of genome covered by SNPs minus gaps > 150kb
Montbéliarde	2 499 500 045 bp	1 919 314 607 bp
Normande	2 499 403 287 bp	1 919 653 803 bp
Holstein	2 499 418 974 bp	1 959 205 780 bp

F_{ROH}

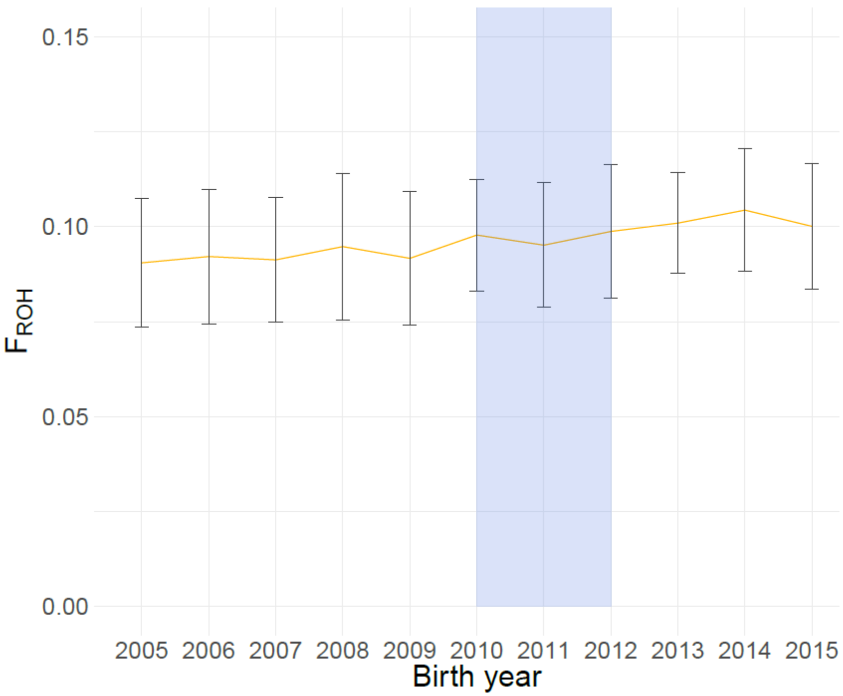
Breed	**F_{ROH}**				
	b_1	Standard error	a_1	Standard error	Relative change
Montbéliarde	1.766E-03	3.935E-04	9.089E-04	8.577E-04	**-0.485 ns**
Normande	1.032E-03	4.021E-04	9.054E-04	7.744E-04	**-0.122 ns**
Holstein	8.730E-04	1.986E-04	5.802E-03	5.218E-04	**5.646 ****

F_{ROH}

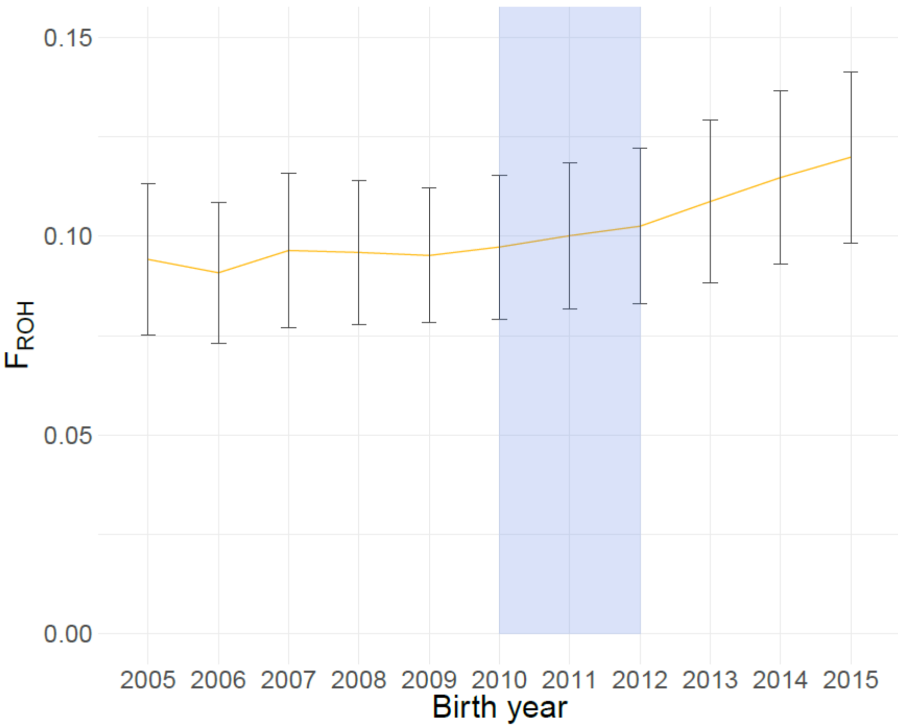
Montbéliarde



Normande



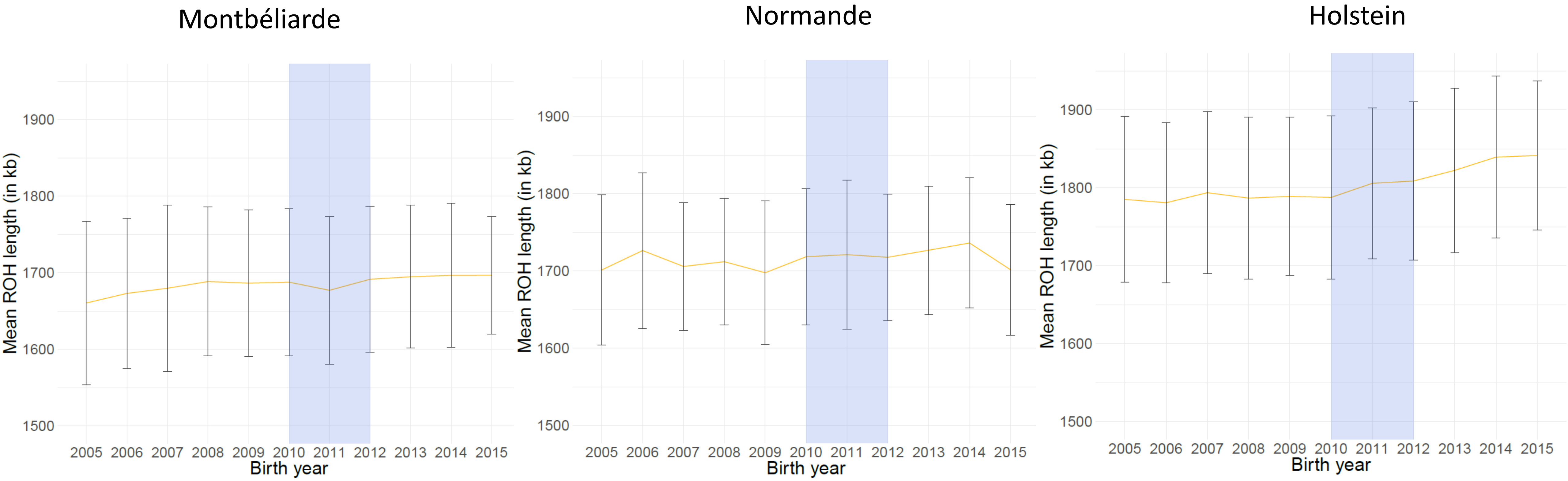
Holstein



ROH length

Breed	Number of ROH per individual				
	b_1	Standard error	a_1	Standard error	Relative change
Montbéliarde	5.447E+00	2.070E+00	1.881E+00	3.859E+00	**-0.655 ns**
Normande	-1.448E-01	2.146E+00	-2.800E+00	4.052E+00	**-18.337 ns**
Holstein	9.838E-01	1.120E+00	1.146E+01	2.550E+00	**10.649 ****

ROH length


Montbéliarde
Normande
Holstein
Mean ROH length (in kb)
1500
1600
1700
1800
1900
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Birth year

Genetic gain

Total Merit Index (ISU): centered around 100 with a 20 points variability

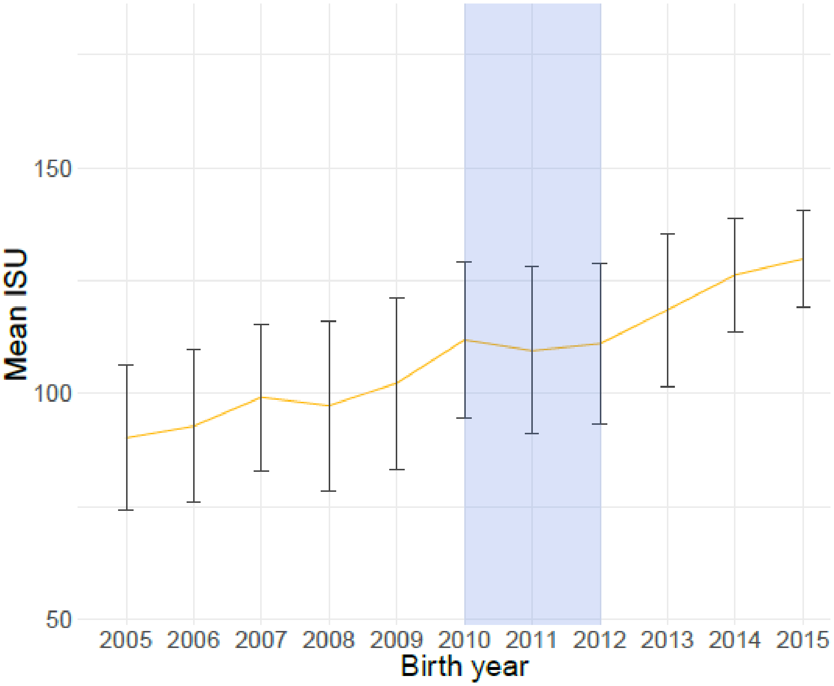
Breed	Milk production	Morphology	Reproduction	Udder health	Longevity	Milking speed
Montbéliarde	45%	12.5%	18%	14.5%	5%	5%
Normande	40%	18%	15.5%	18.5%	5%	3%
Holstein	35%	15%	22%	18%	5%	5%

Genetic gain

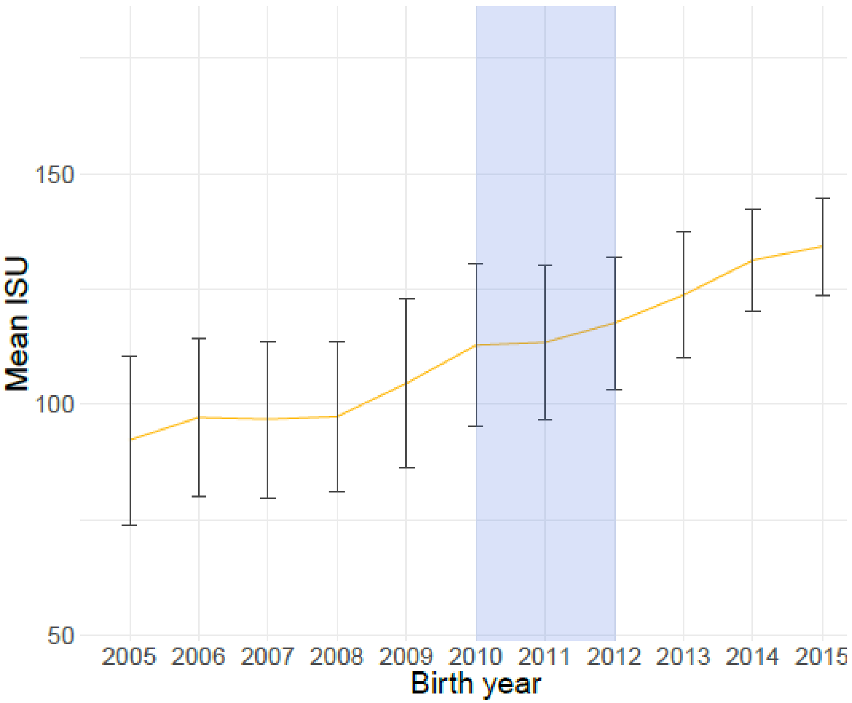
Breed	ISU (Total Merit Index)				
	b_1	Standard error	a_1	Standard error	Relative change
Montbéliarde	3.928	0.355	6.627	0.645	**0.687 ****
Normande	3.411	0.411	5.815	0.612	**0.705 ***
Holstein	7.966	0.200	11.020	0.351	**0.383 ****

Genetic gain

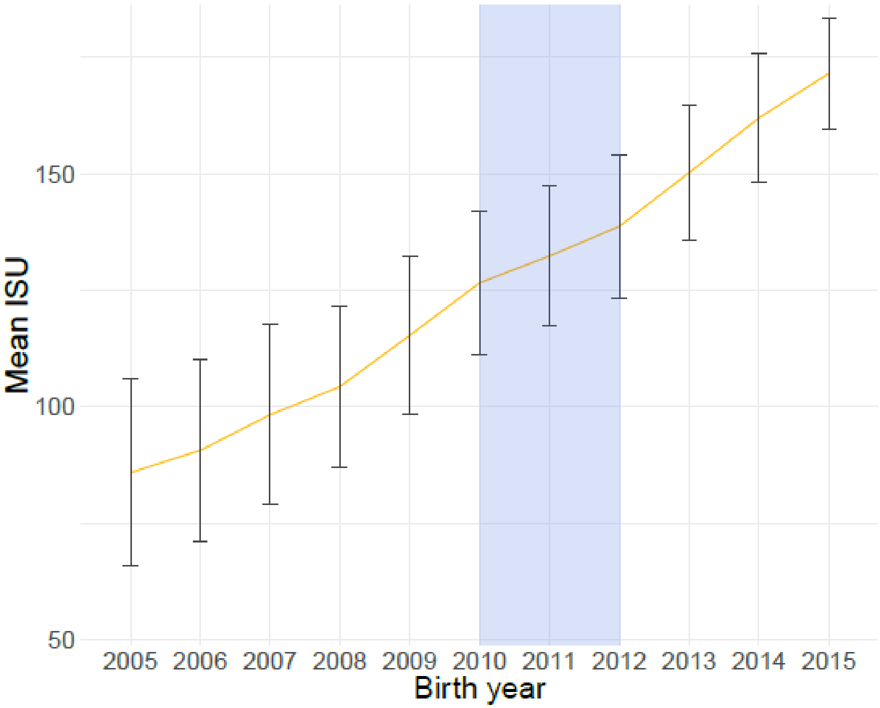
Montbéliarde



Normande



Holstein



Sire's use disequilibrium index

$$\text{Sire's use disequilibrium index} = 1 - \frac{\text{Observed equilibrium}}{\text{Expected equilibrium}}$$

$$\text{Observed equilibrium} = 1 - \sum_{i=1}^{\text{Number of sires } n} \left(\frac{\text{Number of offsprings for sire } i}{\text{Total number of offsprings for the } n \text{ sires}} \right)^2$$

$$\text{Expected equilibrium} = 1 - \sum_{i=1}^{\text{Number of sires } n} \left(\frac{\text{Mean number of offsprings per sire}}{\text{Total number of offsprings for the } n \text{ sires}} \right)^2$$