TOWARDS IMPROVEMENT OF RUMINANT BREEDING THROUGH GENOMIC AND EPIGENOMIC APPROACHES

Changes in genetic correlations due to selection and random drift

Beatriz C.D. Cuyabano[1], Sophie Aguerre[2], Mariana R. Motta[3], and Sophie Mattalia[2]

[1] Université Paris Saclay, INRAE, AgroParisTech, GABI, 78350 Jouy-en-Josas, France

[2] Idele, UMT eBIS, 75012 Paris, France

[3] Department of Statistics, University of Campinas, 13083 Campinas - SP, Brazil

74th EAAP Annual Meeting
30 August, 2023

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101000226

- Selection affects genetic means and variance components,
- Wide knowledge and amount of studies about the effects of selection in genetic variance (Bulmer effect),
- Only a few studies (with limitations) about the effect of selection in genetic correlations,
  - Y. Itoh 1991, *Changes in genetic correlations by index selection*
  - W.G. Hill et al. 1965, *PhD thesis Appendix A: Some observations on assymetrical correlated responses to selection*
  - G.M. Tallis 1987, *Ancestral covariance and the Bulmer effect*

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WHY STUDY EFFECT OF SELECTION ON GENETIC CORRELATIONS?

Breeding programs rely on the selection for multiple traits

↓

Selection index

↓

Depends on genetic correlations between traits

IF GENETIC CORRELATIONS ARE AFFECTED BY SELECTION,

WE SHOULD ACCOUNT FOR THEIR CHANGES WHEN BUILDING

THE SELECTION INDEX FOR THE NEXT GENERATIONS

RUMIGEN - OBJECTIVES

1. **Theory:** develop calculus of $\rho_g^{(t)}$ for populations under selection,
2. **Proof of concept:** simulations to empirically observe the trajectory $\rho_g^{(t)}$,
3. **Real data study:** obtain $\rho_g^{(t)}$ in real data for many generations and interpret the results.

$$\left(\begin{array}{c} \text{Particular interest on negatively correlated traits: trade-off} \\ \text{Study traits known to be affected by increasing temperatures} \end{array} \right)$$

PROOF OF CONCEPT

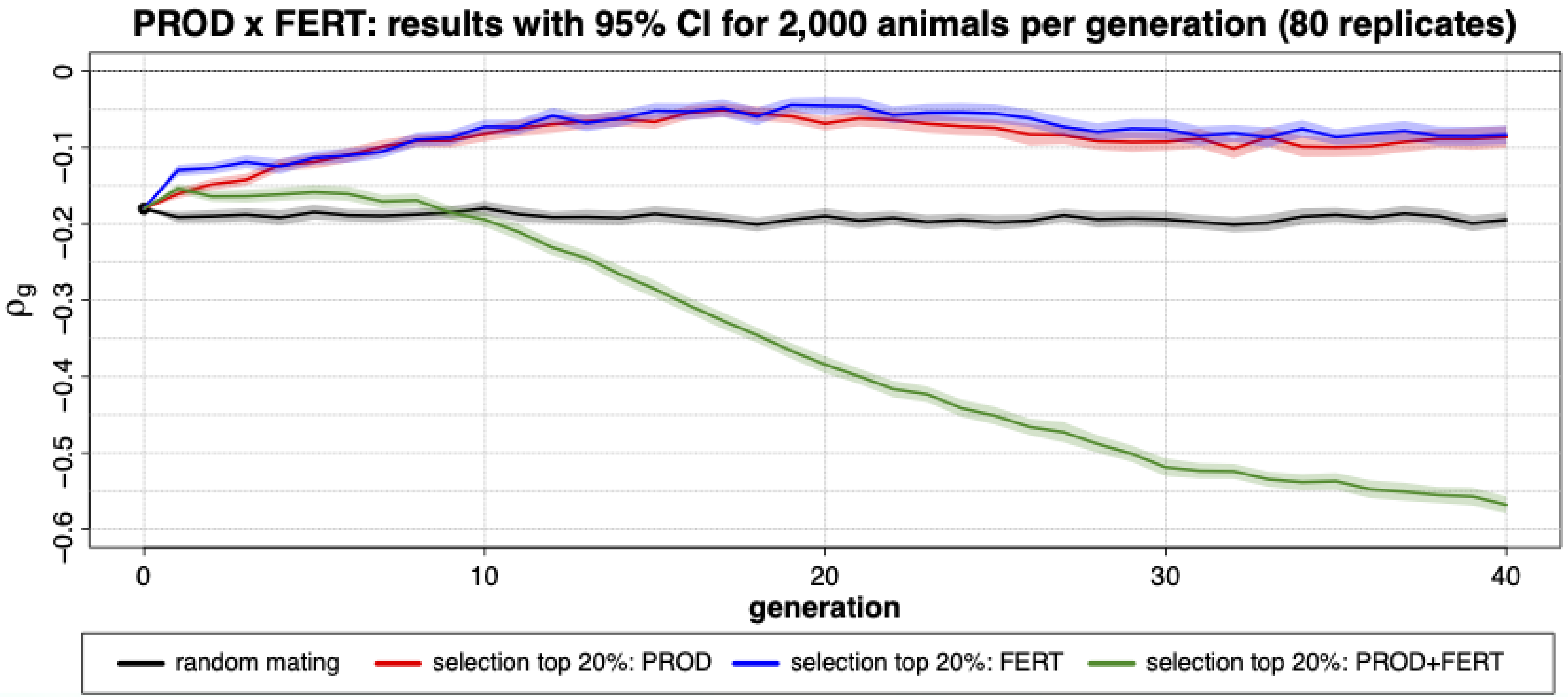
SIMULATION STUDY

RUMIGEN - SIMULATION STUDY parameters

- Two negatively correlated traits: production and fertility,
  - PROD with $h^2 = 0.3$; FERT with $h^2 = 0.01$
  - 1,500 QTL to generate the breeding values for both traits: 500 shared and 500 trait specific,
  - $\rho_g = -0.2 \xrightarrow[t \to 10 \text{ (random mating)}]{} \rho_g^{(0)} = -0.18.$
- Four scenarios of selection (top 20% best individuals) over 40 generations:
  - Random mating (*i.e.* no selection),
  - Selection only for PROD,
  - Selection only for FERT,
  - Selection for both PROD and FERT.
- 2,000 individuals per generation.

Note: selection and calculus of $\hat{\rho}_g$ per generation were made on true breeding values.

RUMIGEN - SIMULATION STUDY results



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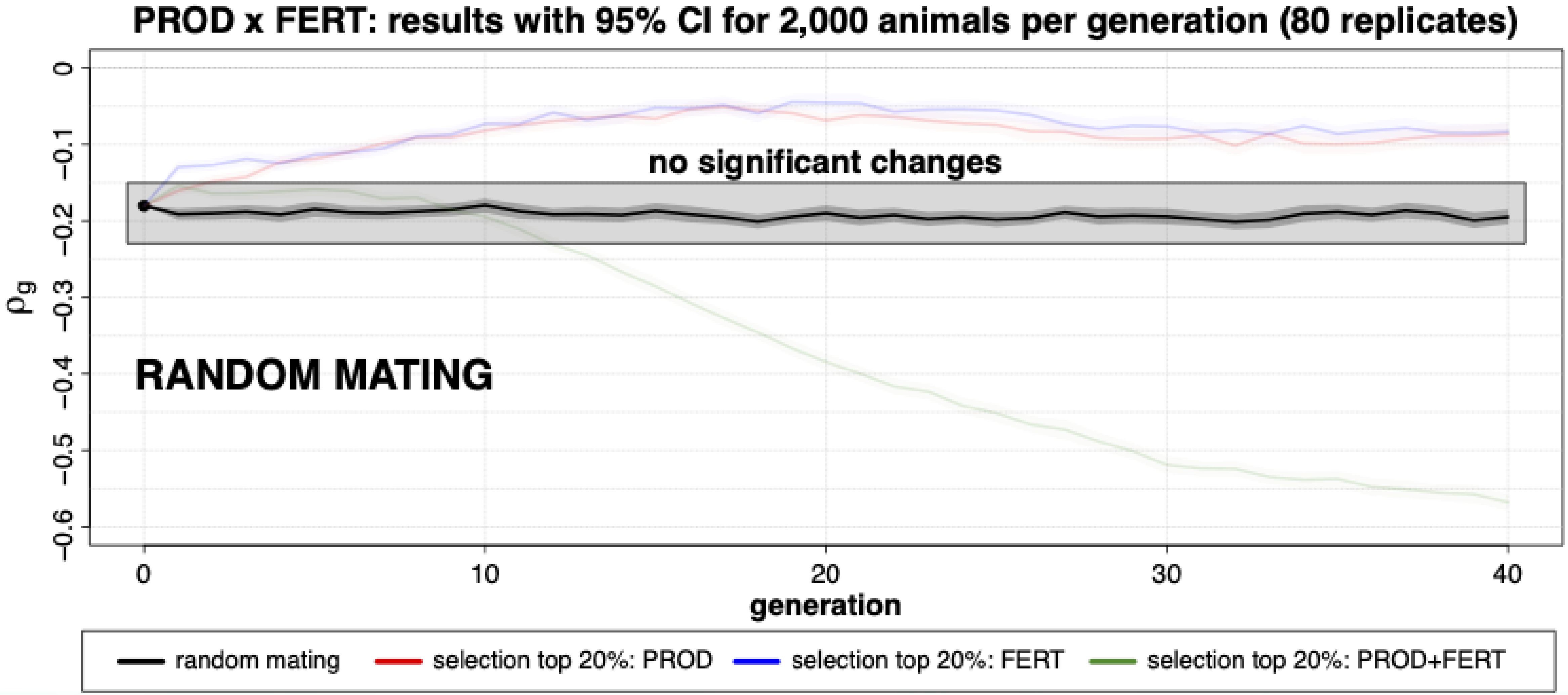

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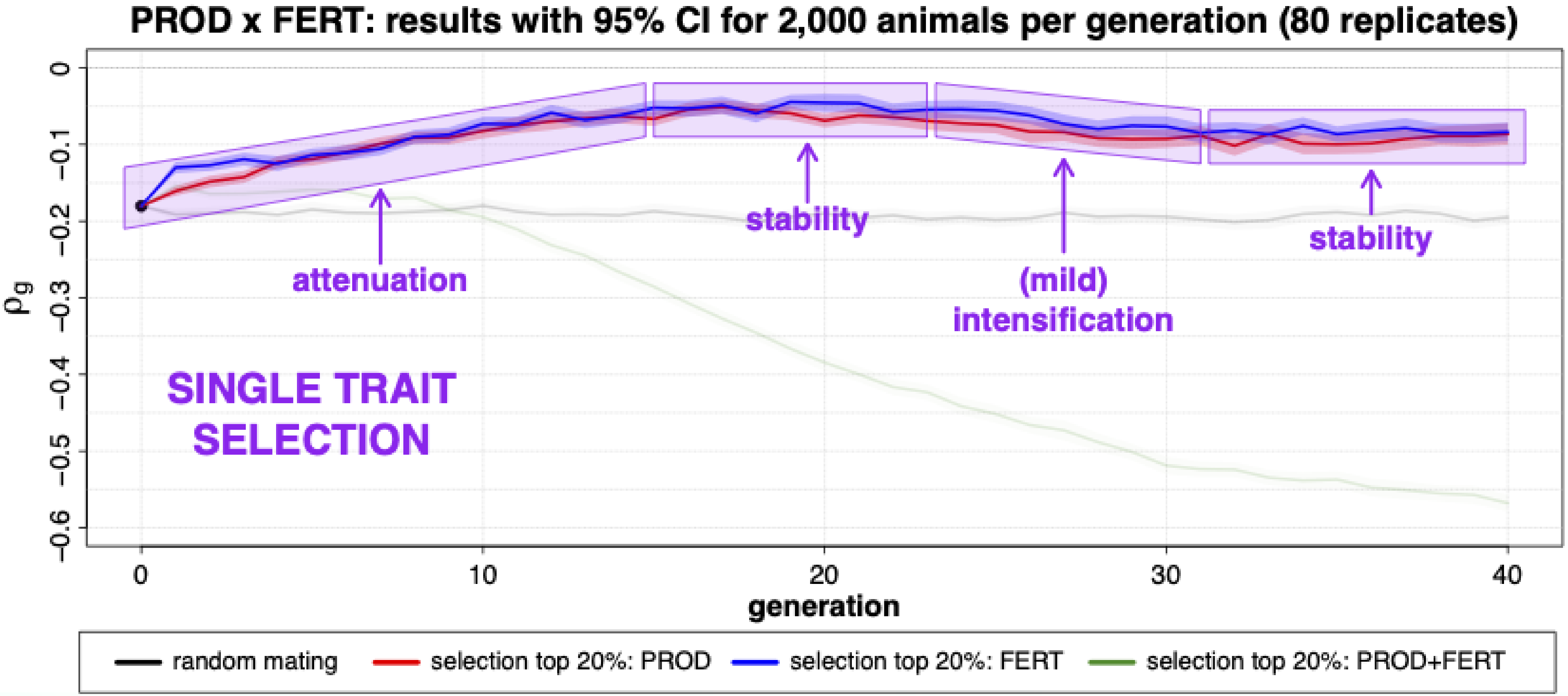

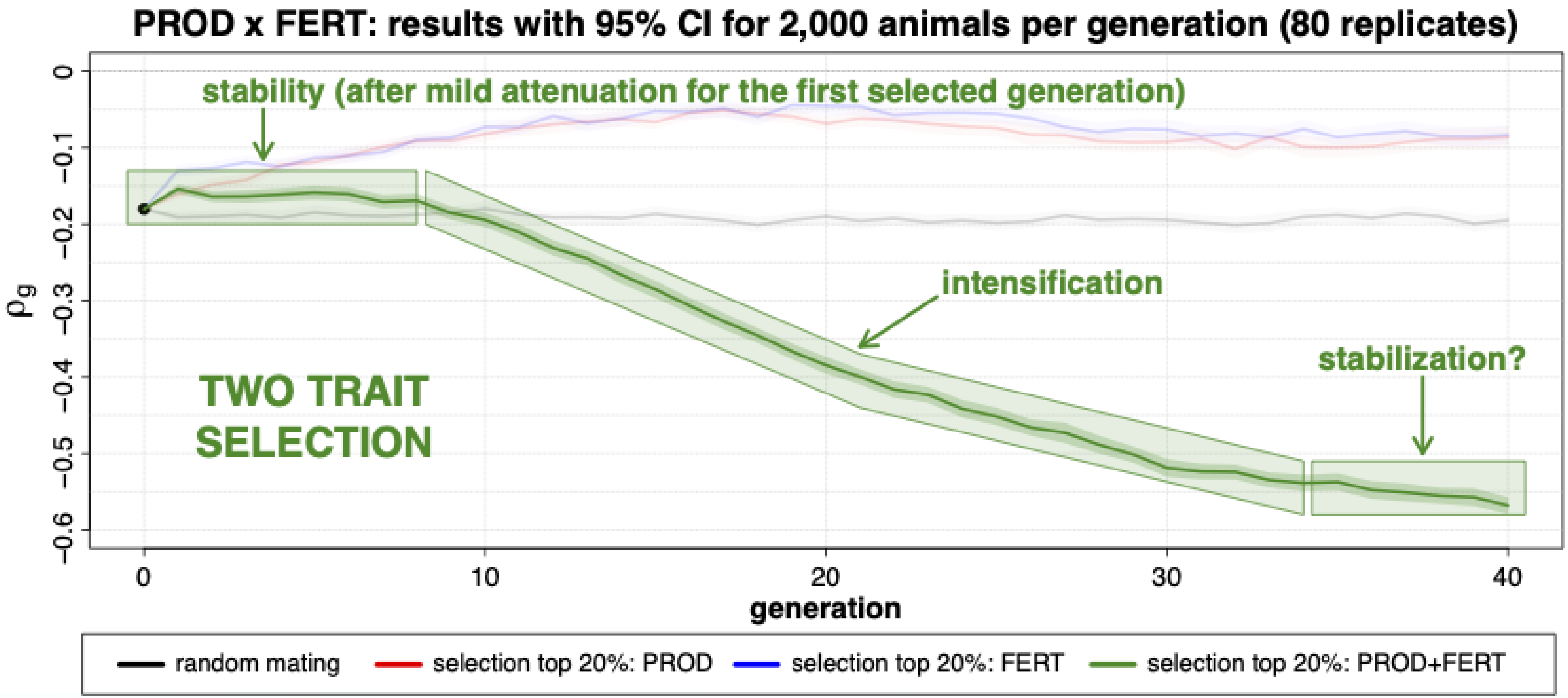
PROD x FERT: results with 95% CI for 2,000 animals per generation (80 replicates)
stability (after mild attenuation for the first selected generation)
intensification
stabilization?
TWO TRAIT SELECTION
ρg
0
−0.1
−0.2
−0.3
−0.4
−0.5
−0.6
0
10
20
30
40
generation
random mating
selection top 20%: PROD
selection top 20%: FERT
selection top 20%: PROD+FERT

THEORY

CALCULUS OF $\rho_g^{(t)}$

RUMIGEN - CALCULUS OF $\rho_g^{(t)}$ selection and random drift

$$\boxed{\rho_g^{(t)} = \frac{\sigma_{g12}^{(t)}}{\sqrt{\sigma_{g_1}^{2(t)}\sigma_{g_2}^{2(t)}}}}$$

RUMIGEN - CALCULUS OF $\rho_g^{(t)}$ selection and random drift

$$\boxed{\rho_g^{(t)} = \frac{\sigma_{g12}^{(t)}}{\sqrt{\sigma_{g_1}^{2(t)}\sigma_{g_2}^{2(t)}}}}$$

- Changes in genetic variances and covariance can be separated as changes due to selection (δ_{sel}) and random drift (δ_{drift}):

$$\boxed{\rho_g^{(t)} = \frac{\sigma_{g12}^{(0)}\left[1-\delta_{sel_{12}}^{(t)}-\delta_{drift_{12}}^{(t)}\right]}{\sqrt{\sigma_{g_1}^{2(0)}\left[1-\delta_{sel_1}^{(t)}-\delta_{drift_1}^{(t)}\right]\sigma_{g_2}^{2(0)}\left[1-\delta_{sel_2}^{(t)}-\delta_{drift_2}^{(t)}\right]}} = \rho_g^{(0)}\frac{\left[1-\delta_{sel_{12}}^{(t)}-\delta_{drift_{12}}^{(t)}\right]}{\sqrt{\left[1-\delta_{sel_1}^{(t)}-\delta_{drift_1}^{(t)}\right]\left[1-\delta_{sel_2}^{(t)}-\delta_{drift_2}^{(t)}\right]}}}$$

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- $\delta_{sel}^{(t)}$: moments of BVs $g_1^{(t-1)}, g_2^{(t-1)} \sim \mathcal{N}_2(\mathbf{0}, \mathbf{\Sigma}^{(t)} \otimes \boldsymbol{G})$ conditional on selection,
- $\delta_{drift}^{(t)} = \bar{A}_{ij}^{(t)} + \bar{F}_i^{(t)}$ (Sorensen et al.; 2001, Macedo et al.,2021).

RUMIGEN - CALCULUS OF $\rho_g^{(t)}$ selection and random drift

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- $\delta_{sel}^{(t)} \rightarrow d_{sel}$ after a number of selected generations,
- $\delta_{drift}^{(t)}$ is negligible at initial generations under selection.

THEORY

INTERPRETATION OF $\rho_g^{(t)}$

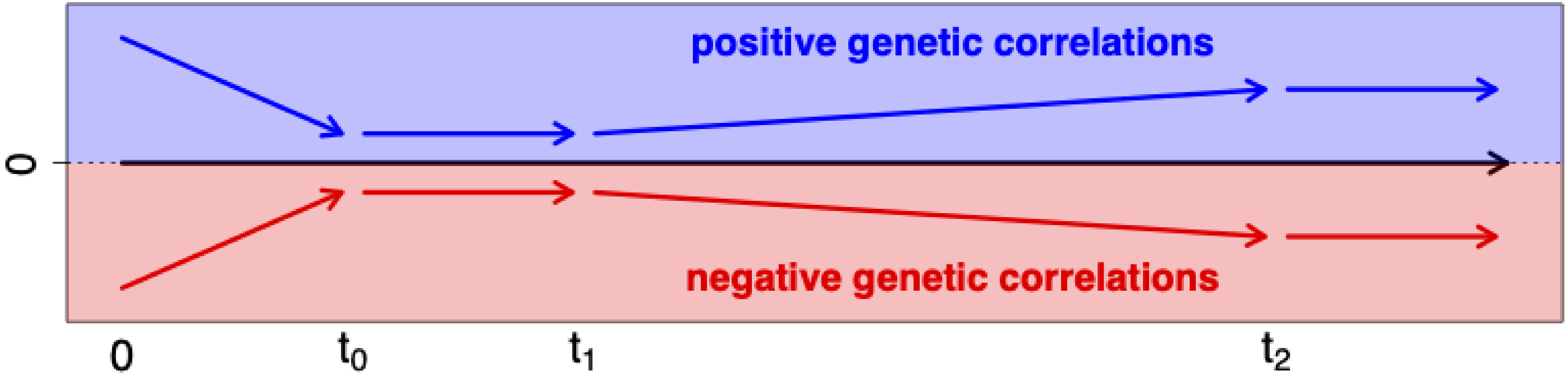
RUMIGEN - INTERPRETATION OF $\rho_g^{(t)}$ selection for a single trait

$$\boxed{\rho_g^{(t)} = \rho_g^{(0)} \frac{\left[1-\delta_{sel_{12}}^{(t)} - \delta_{drift_{12}}^{(t)}\right]}{\sqrt{\left[1-\delta_{sel_1}^{(t)} - \delta_{drift_1}^{(t)}\right]\left[1-\delta_{sel_2}^{(t)} - \delta_{drift_2}^{(t)}\right]}}}$$

- Changes on σ_g^2 of selected trait 1: $\delta_{sel_1}^{(t)} = \delta_{sel}^{(t)}$ and $\delta_{drift_1}^{(t)} = \delta_{drift}^{(t)}$,
- Changes on σ_g^2 of correlated trait 2: proportional to $\left[\rho_g^{(0)} \ldots \rho_g^{(t-1)}\right]^2$ (both $\delta_{sel_2}^{(t)}$ and $\delta_{drift_2}^{(t)}$),
- Changes on covariance: $\delta_{sel_{12}}^{(t)} = \delta_{sel}^{(t)}$; proportional to $\left|\rho_g^{(0)} \ldots \rho_g^{(t-1)}\right|$ on $\delta_{drift_{12}}^{(t)}$

RUMIGEN - INTERPRETATION OF $\rho_g^{(t)}$ selection for a single trait

$$\rho_g^{(t)} = \rho_g^{(0)} \frac{\left[1-\delta_{sel_{12}}^{(t)}-\delta_{drift_{12}}^{(t)}\right]}{\sqrt{\left[1-\delta_{sel_1}^{(t)}-\delta_{drift_1}^{(t)}\right]\left[1-\delta_{sel_2}^{(t)}-\delta_{drift_2}^{(t)}\right]}}$$



$\delta_{sel}^{(t)} < d_{sel}$	$\delta_{sel}^{(t)} \longrightarrow d_{sel}$	
$\delta_{drift}^{(t)} \approx 0$	$\delta_{drift}^{(t)} > 0$	$\delta_{drift}^{(t)} \longrightarrow d_{drift}$

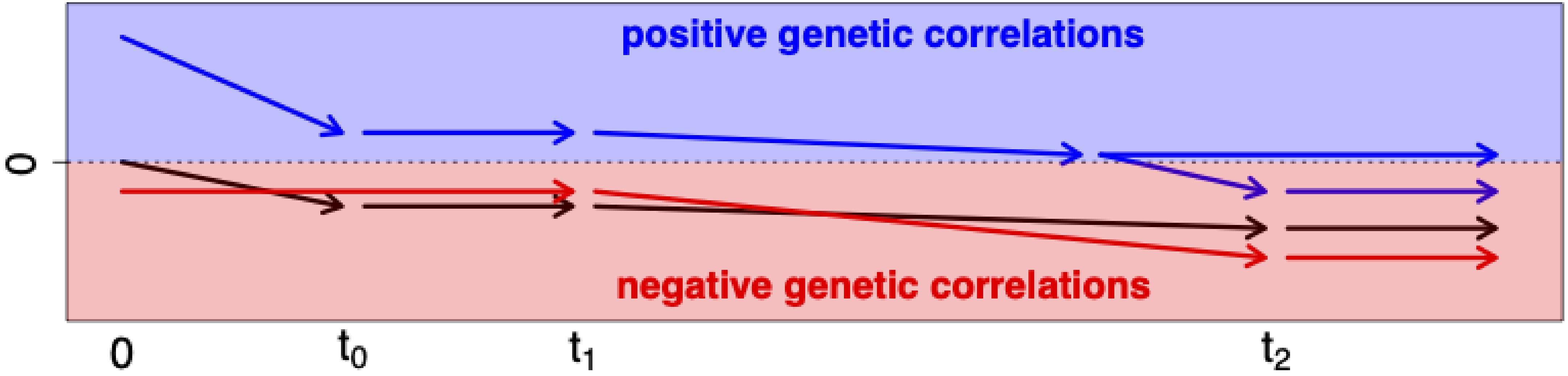
RUMIGEN - INTERPRETATION OF $\rho_g^{(t)}$ selection for both traits

$$\boxed{\rho_g^{(t)} = \rho_g^{(0)} \frac{\left[1-\delta_{sel_{12}}^{(t)}-\delta_{drift_{12}}^{(t)}\right]}{\sqrt{\left[1-\delta_{sel_1}^{(t)}-\delta_{drift_1}^{(t)}\right]\left[1-\delta_{sel_2}^{(t)}-\delta_{drift_2}^{(t)}\right]}}}$$

- Changes on σ_g^2 due to selection: $\delta_{sel_1}^{(t)} \propto i_1^{(t)} + i_2^{(t)} \left[\rho_g^{(0)} \dots \rho_g^{(t-1)}\right]^2,$
  $\delta_{sel_2}^{(t)} \propto i_2^{(t)} + i_1^{(t)} \left[\rho_g^{(0)} \dots \rho_g^{(t-1)}\right]^2,$
- Changes on σ_g^2 due to drift: $\delta_{drift}^{(t)} = \delta_{drift_1}^{(t)} \approx \delta_{drift_2}^{(t)},$
- Changes on covariance: $\delta_{sel_{12}}^{(t)} \propto i_1 + i_2,$
  $\delta_{drift_{12}}^{(t)} \approx \left|\rho_g^{(0)} \dots \rho_g^{(t-1)}\right| \delta_{drift}^{(t)}.$

RUMIGEN - INTERPRETATION OF $\rho_g^{(t)}$ selection for both traits

$$\rho_g^{(t)} = \rho_g^{(0)} \frac{\left[1-\delta_{sel_{12}}^{(t)}-\delta_{drift_{12}}^{(t)}\right]}{\sqrt{\left[1-\delta_{sel_1}^{(t)}-\delta_{drift_1}^{(t)}\right]\left[1-\delta_{sel_2}^{(t)}-\delta_{drift_2}^{(t)}\right]}}$$



$\delta_{sel}^{(t)} < d_{sel}$	$\delta_{sel}^{(t)} \longrightarrow d_{sel}$

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REAL DATA STUDY

French Montbéliard data

- 30 years of records (1992-2021) from first lactation:
  - PROD (MY305d / FY305d / PY305d)
  - FERT (CR at first insemination after the start of lactation)
- $\approx$ 810,000 cows with complete records on PROD/FERT,
- $\approx$ 4 million animals in pedigree.

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Model for genetic evaluation

$$\boldsymbol{y} = \boldsymbol{X}\beta + \text{AI bull} + \boldsymbol{g} + \boldsymbol{e} \longrightarrow \mathcal{N}(0, \boldsymbol{R}\sigma_e^2)$$

$\boldsymbol{X}\beta$: fixed effects

AI bull: FERT only: $\mathcal{N}(0, \boldsymbol{I}\sigma^2_{bull\times year})$

$\boldsymbol{g}$: $\mathcal{N}(0, \boldsymbol{A}\sigma_g^2)$

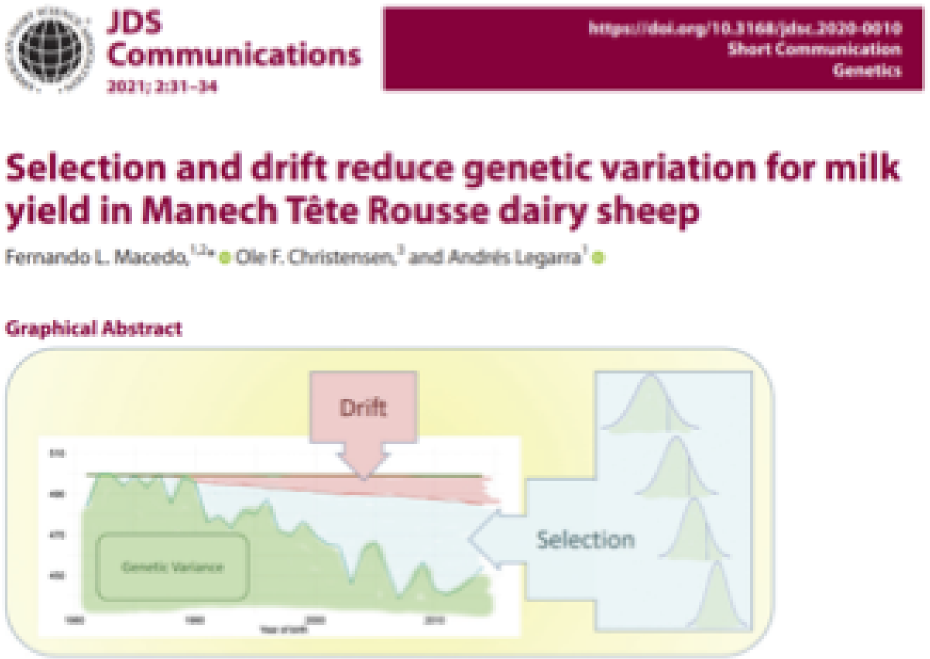
$\boldsymbol{e}$: (het. variance by HY group)

Fixed effects:

- overall mean, age, HYS
- PROD: lactation length
- FERT: L1-AI interval
  sexed semen
  AI operator
  day of the week

RUMIGEN - REAL DATA STUDY methodology to estimate $\rho_g^{(t)}$

- Follow methodology proposed by Macedo et al. (2021) to estimate $\sigma_g^{2(t)}$:


JDS Communications
2021; 2:31–34

https://doi.org/10.3168/jdsc.2020-0010
Short Communication
Genetics

Selection and drift reduce genetic variation for milk yield in Manech Tête Rousse dairy sheep

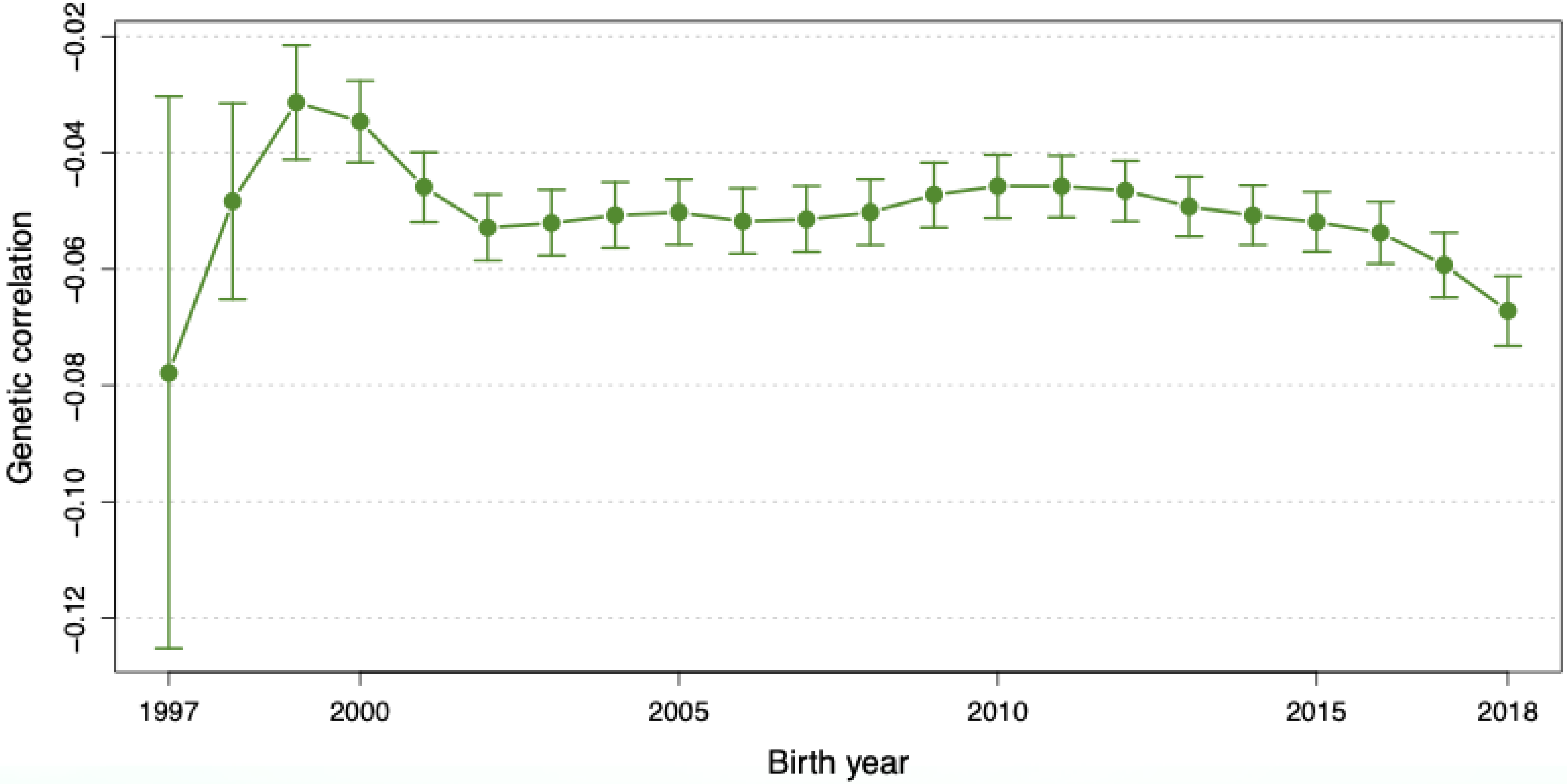
Fernando L. Macedo,[1,2*] Ole F. Christensen,[3] and Andrés Legarra[1]

Graphical Abstract

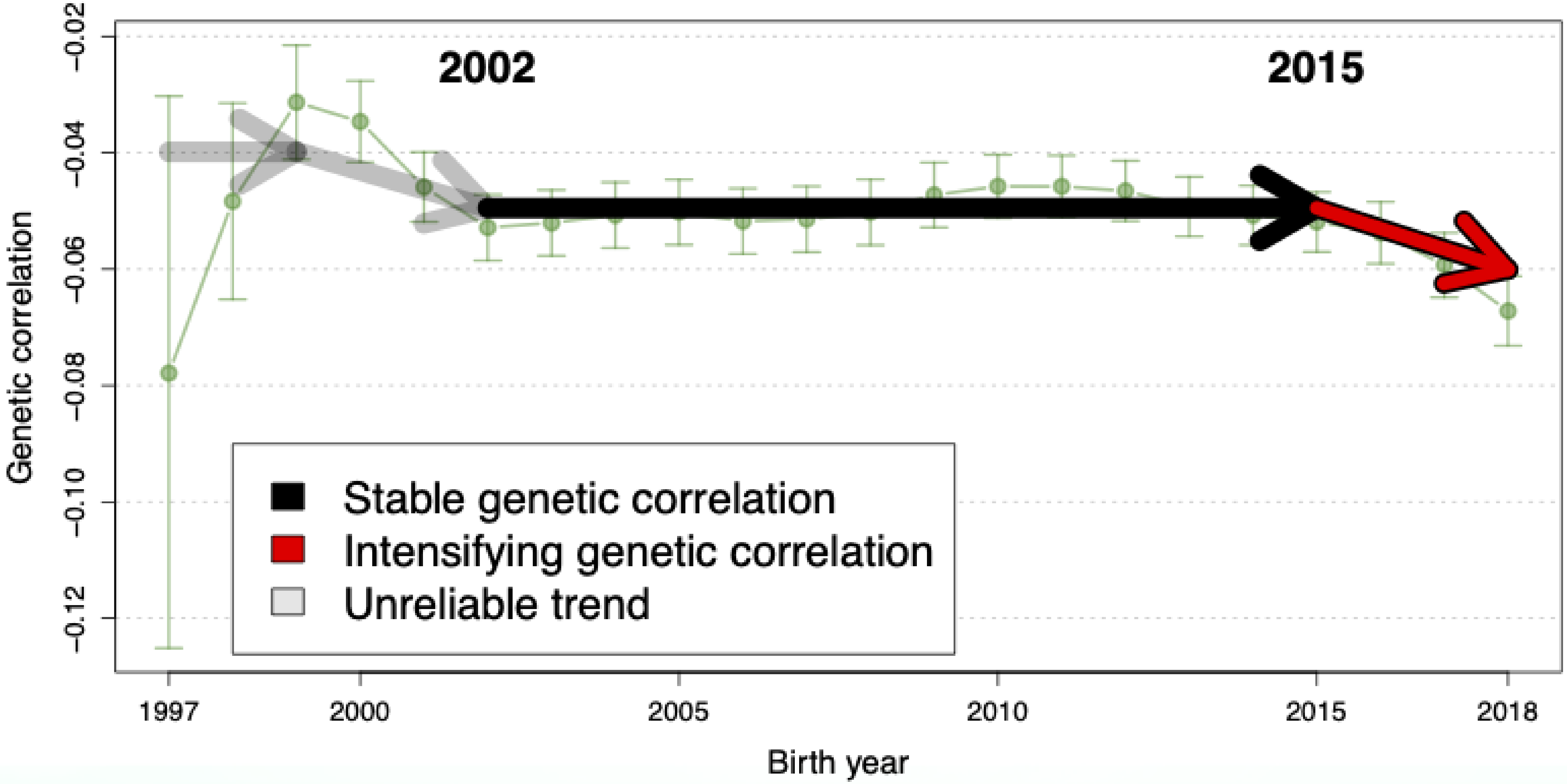
  - Use Gibbs sampler to generate very long MCMC chains with large thinning,
  - Create many samples of breeding values,
  - Use these samples to estimate $\sigma_g^{2(t)}$.

- Extend to two-trait models to estimate the genetic correlations in our data.

RUMIGEN - REAL DATA STUDY preliminary results MY305d × FERT



RUMIGEN - REAL DATA STUDY preliminary results MY305d × FERT



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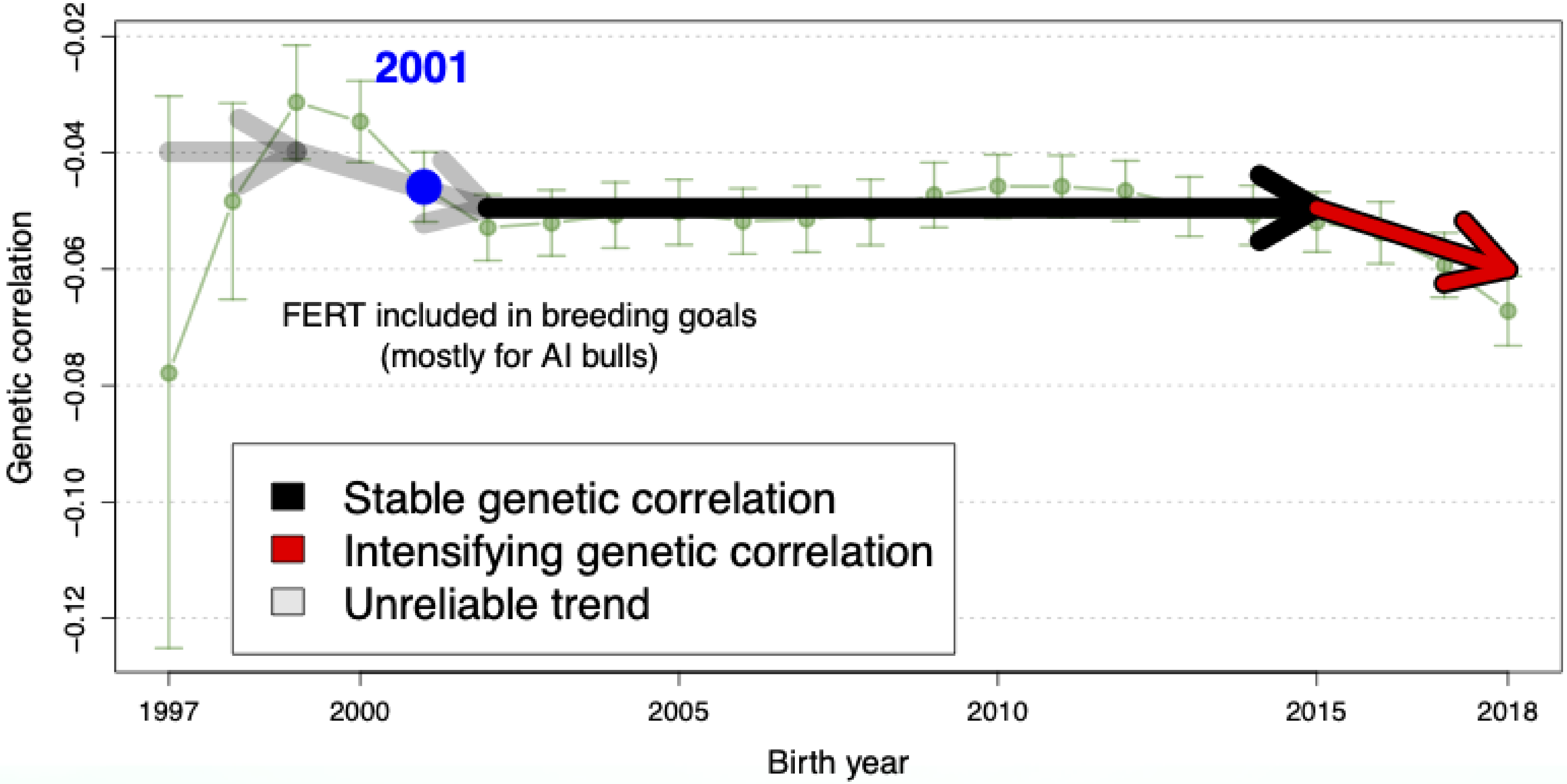
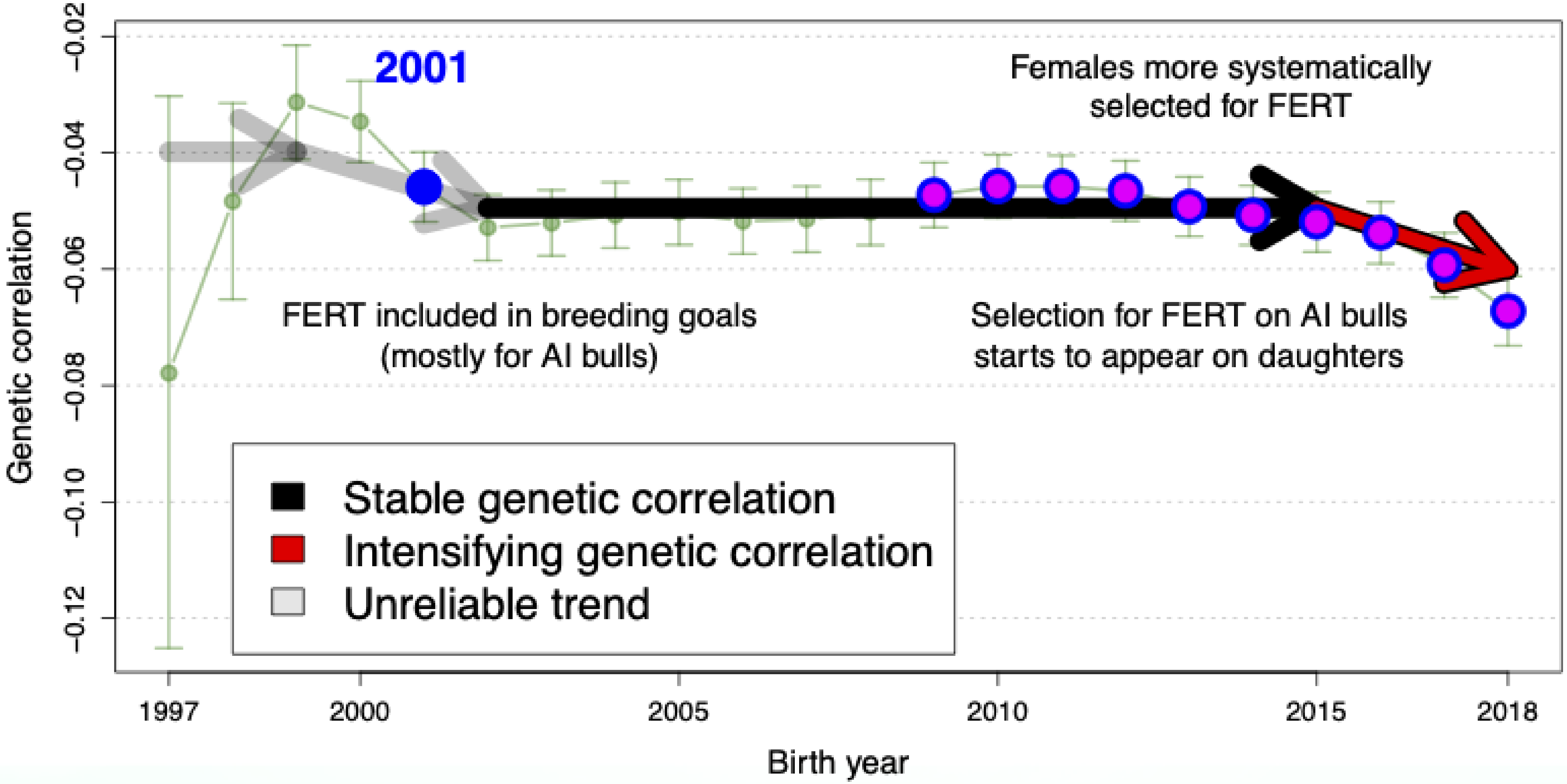
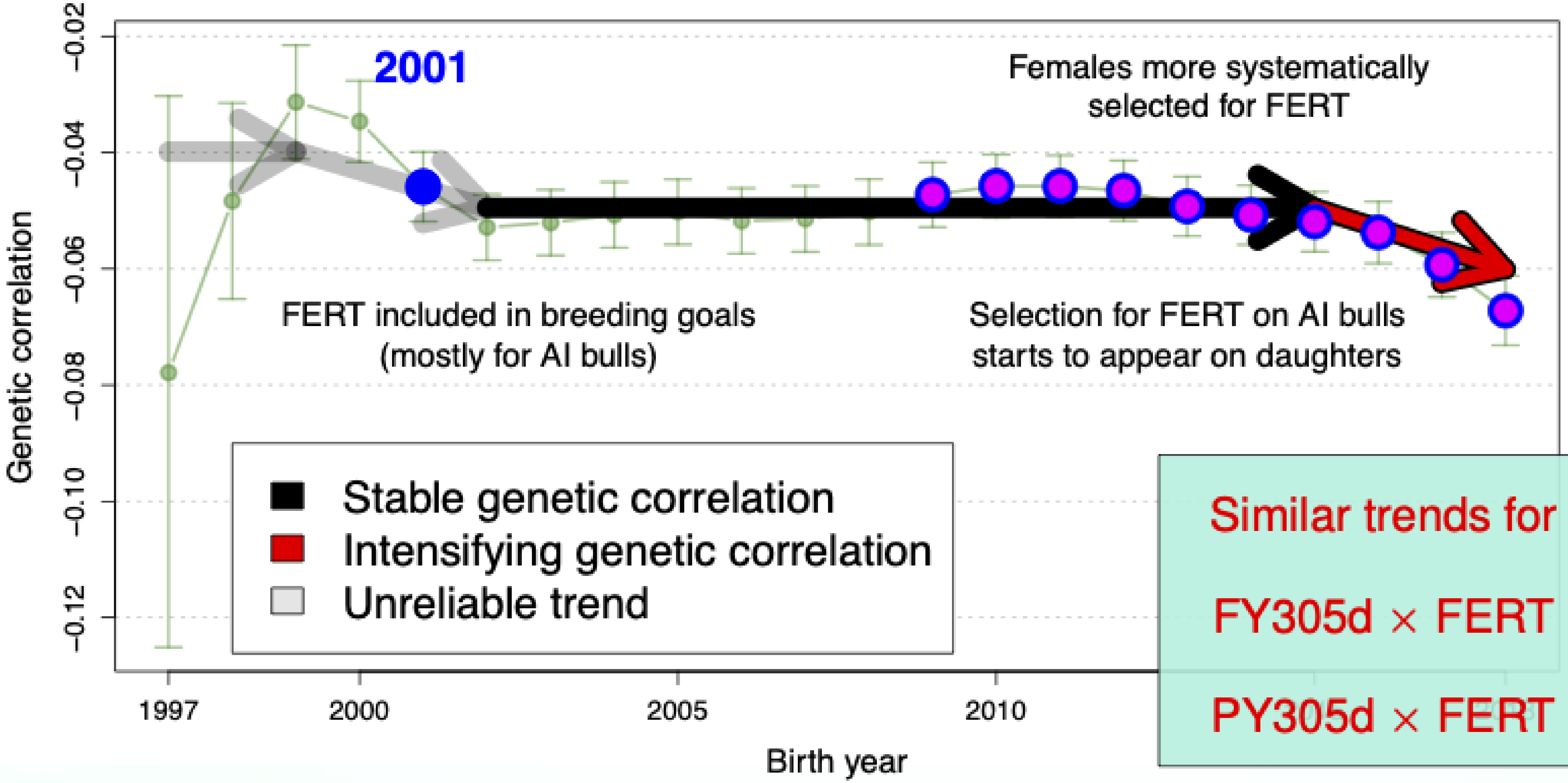


RUMIGEN - REAL DATA STUDY preliminary results MY305d × FERT



RUMIGEN - REAL DATA STUDY preliminary results MY305d × FERT

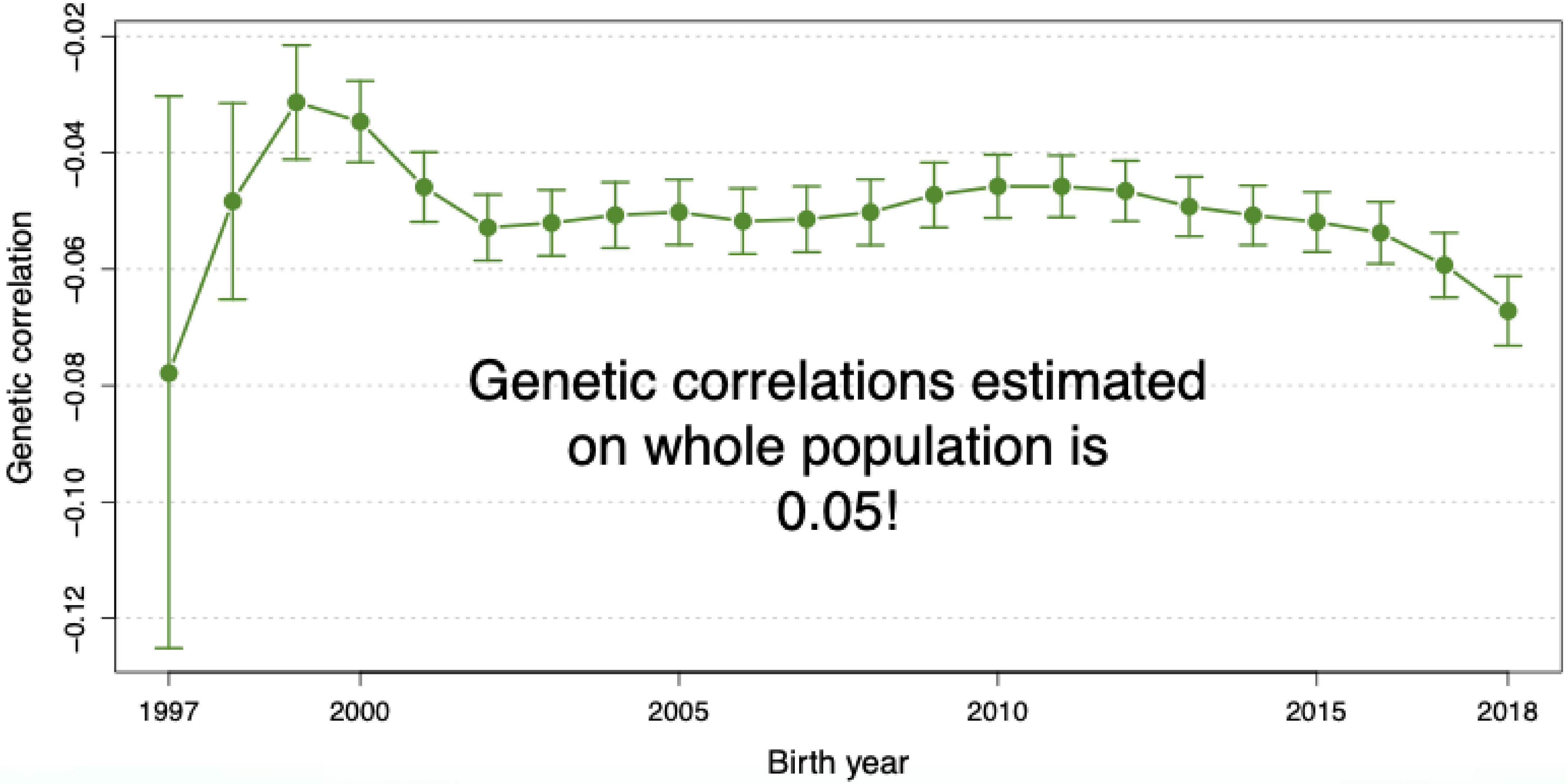


Similar trends for

FY305d × FERT

PY305d × FERT

RUMIGEN - REAL DATA STUDY preliminary results MY305d × FERT



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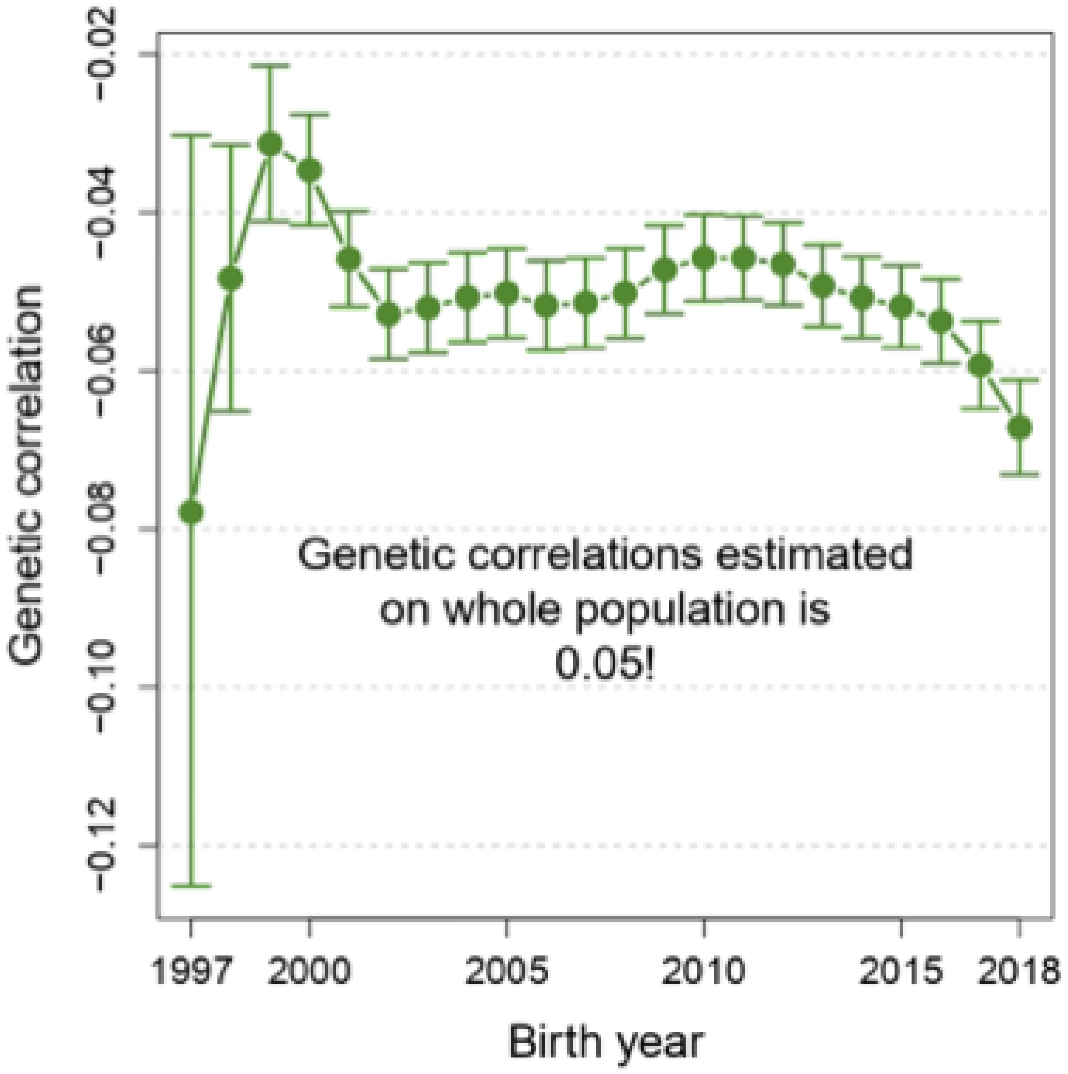

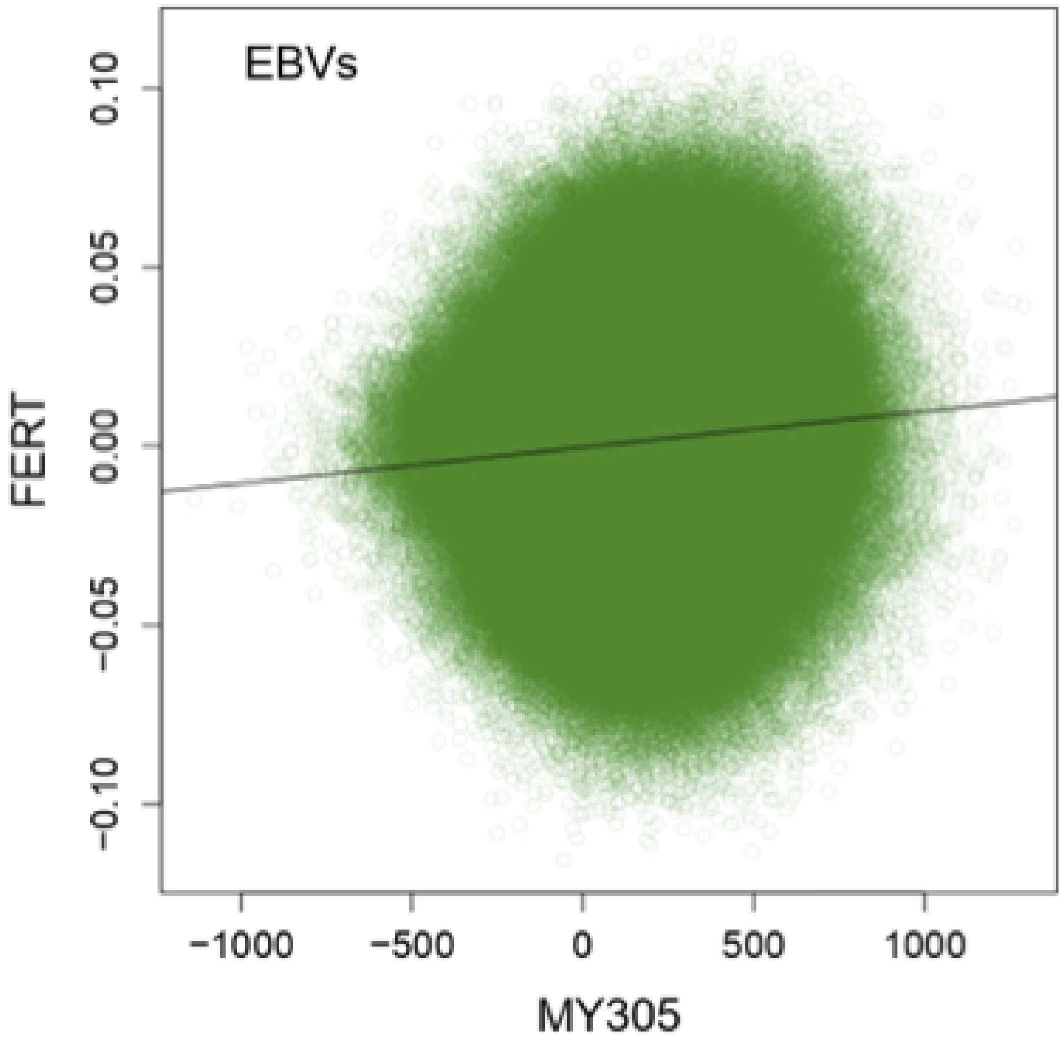

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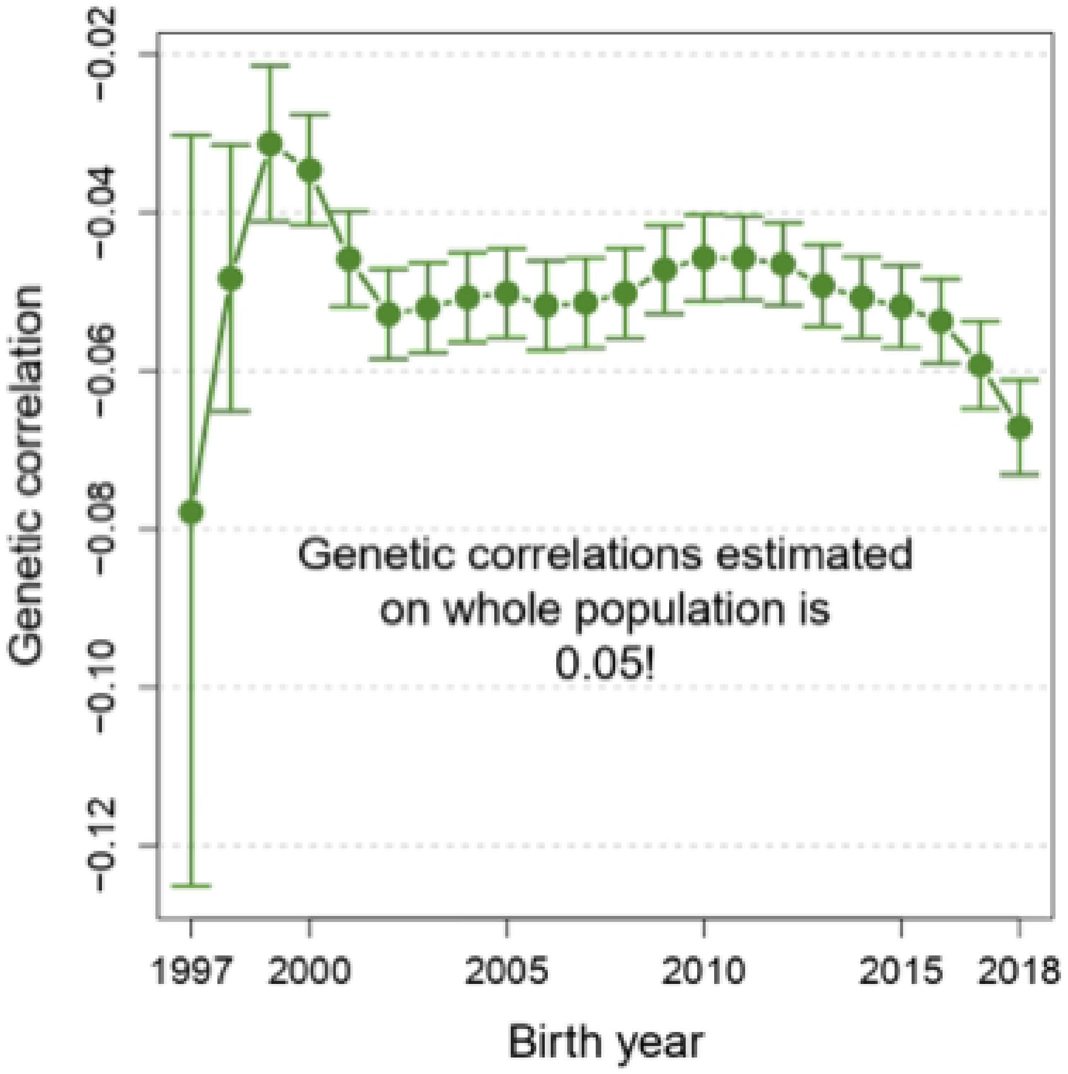

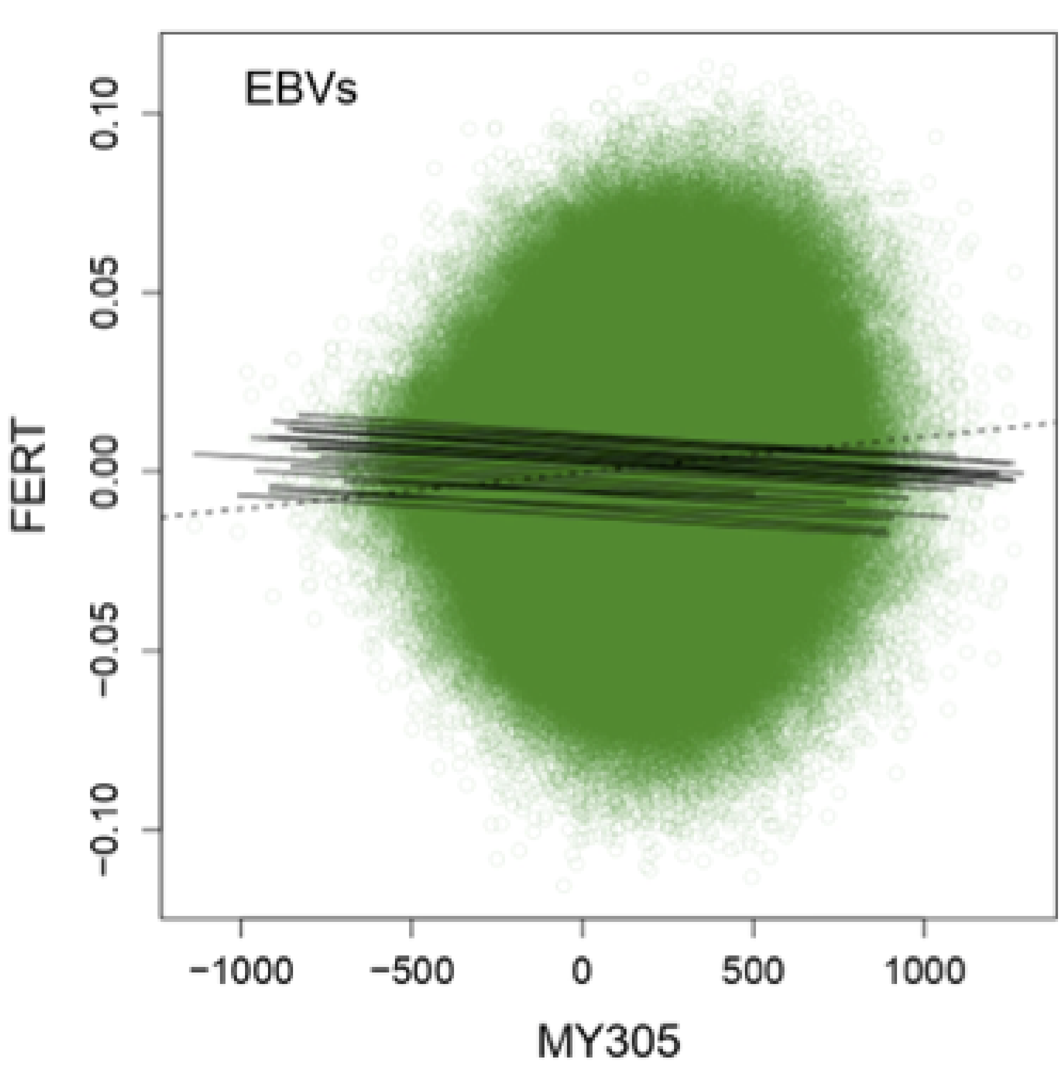

FINAL CONSIDERATIONS

RUMIGEN - FINAL CONSIDERATIONS

- ρ_g is unlikely to be eliminated,
- Simulation study: in the long run simultaneous selection for negatively correlated traits intensifies this correlation,
- Trajectory of ρ_g is strongly related to stage of selection and breeding goals,
- Impact of selection on traits that are not routinely measured is so far unknown, but we can make inferences, based on the expected theoretical trajectory of ρ_g,
- Theory can be used to draw scenarios for traits associated to thermo-tolerance, with the knowledge of current breeding goals.

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Exploring non-linear genetic relationships between correlated traits.
Fatima Shokor et al.
Session 69. Methods and genomic prediction.

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THANK YOU

RUMIGEN PARTNERS

AARHUS UNIVERSITY

CSIC

Danmarks Tekniske Universitet DTU

EAAP European Federation of Animal Science

EFFAB European Forum of Farm Animal Breeders

ELIANCE Des éleveurs. Une ambition.

INSTITUT DE L'ELEVAGE idele

INIA Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria

INRAE

INRAE transfert

IRIAF

LIÈGE université

NMBU

TEKNOLOGIRÅDET DANISH BOARD OF TECHNOLOGY

THE UNIVERSITY OF EDINBURGH

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101000226