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Combining dynamic epidemiological and genetic models to assess the impact of genetic selection strategies on the spread of classical scrapie within a sheep flock

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Introduction

Classical scrapie is a transmissible spongiform encephalopathy that affects small ruminants. Due to potential health risks, it is submitted to eradication measures. It is characterised in sheep by a **genetic factor** based on the PrP major susceptibility gene. Therefore, control strategies partly rely on selective breeding.

Scrapie transmission mechanisms are still incompletely understood. The **long infectious and undetectable incubation period** makes direct data analyses difficult, hence the interest of a modelling approach.

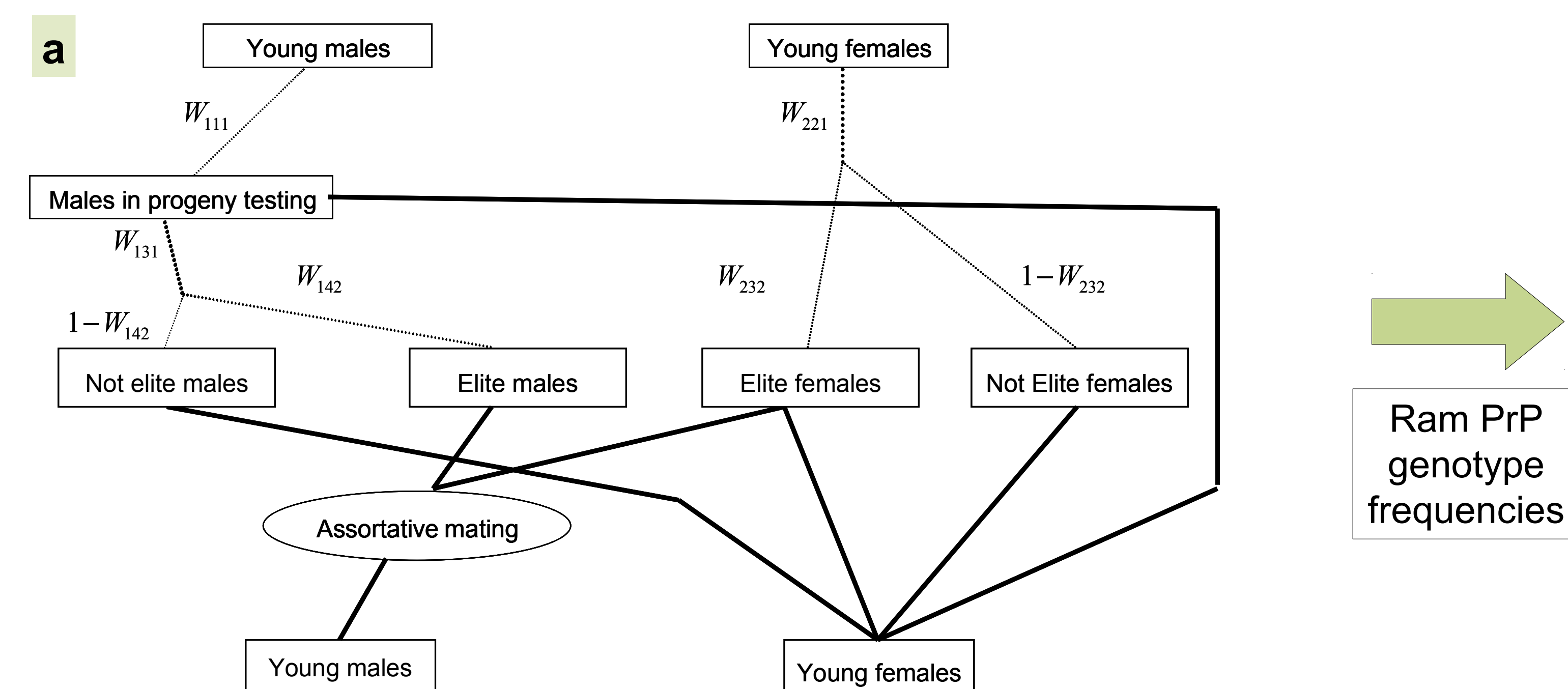
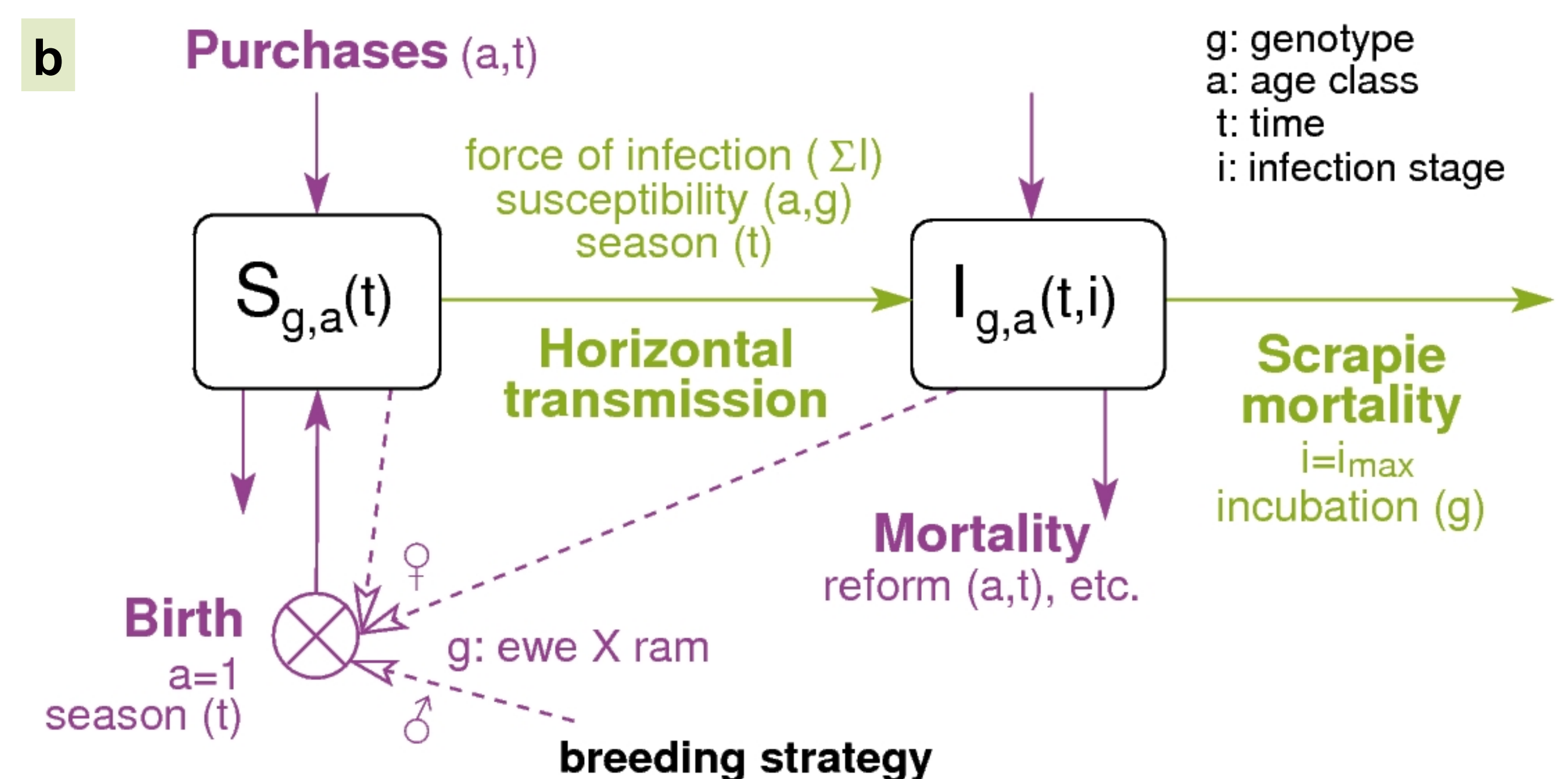


FIG 1. a- Genetic model. Population description with 7 categories (rectangles), 7 matings paths (thick lines), selection steps (dotted lines) and selection proportion W_{sac} (sex $s=1$: males, 2 :females; age $a=1, \dots, a_s$; category $c=1$: not elite, 2: elite).



b- Epidemiological model. Flock of susceptible (S) and infected (I) renewal ewes, structured by genotype (g), age class (a), and infection stage (i); demographic (purple) and epidemiological (green) processes.

Modelling

The **genetic deterministic dynamic model** (FIG 1.a) [1] represents breeding programs including:

- overlapping generations,
- different selection steps,
- different strategies for males and females,
- non-random mating.

It maximises scrapie resistance, with a constraint on loss of genetic progress in milk production.

The **realistic SI-based epidemiological model** (FIG 1.b) [2] takes into account demographic and epidemiological processes, including:

- seasonality in breeding and transmission,
- stochastic mating,
- genetic and age-dependent susceptibilities,
- long and variable incubation periods, etc.

It was calibrated using French outbreak data.

Results

The model was applied to 3 French dairy flocks corresponding to breeds exhibiting contrasting PrP genotype frequencies: Lacaune (FIG 2.A), MTN (FIG 2.B), MTR (FIG 2.C). It was simulated for 9 scenarios combining:

- 3 scrapie introduction scenarios,
- 3 breeding strategies.

The robustness of the results was tested by a **sensitivity analysis**.

➔ Parameters with the greatest impact on the incidence levels and patterns:

- the transmission scaling factor;
- the flock;
- the age and genetic susceptibilities.

Conclusion

Breeding strategies have a strong impact on the disease outbreak and are therefore an **efficient tool to control scrapie**. However, their efficacy in terms of disease eradication strongly depends on the scrapie introduction scenarios.

These results hence emphasise the contribution of our **original approach**, which **combines genetic and epidemiological models in a realistic framework**.

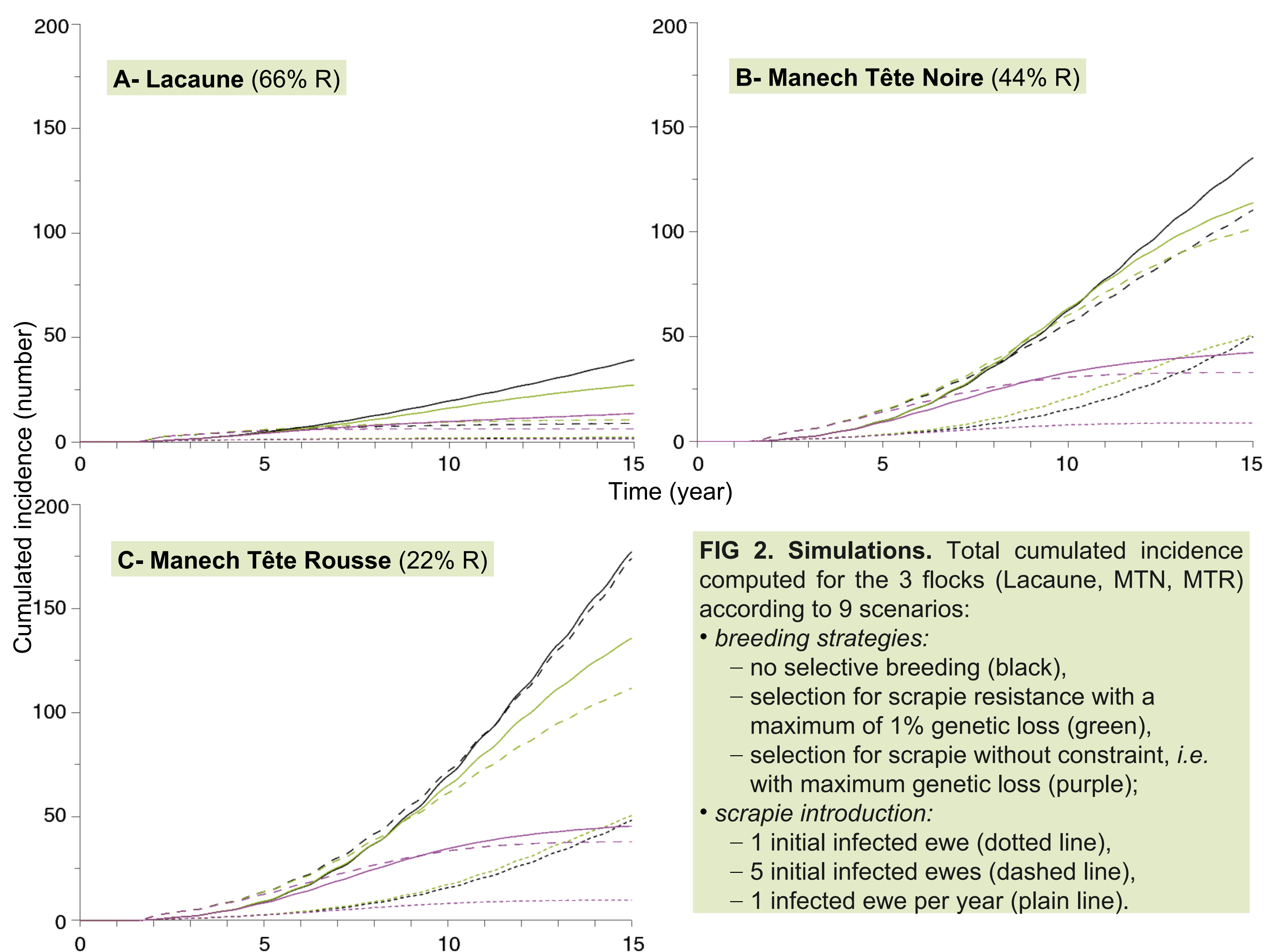


FIG 2. Simulations. Total cumulated incidence computed for the 3 flocks (Lacaune, MTN, MTR) according to 9 scenarios:

- **breeding strategies:**
 - no selective breeding (black),
 - selection for scrapie resistance with a maximum of 1% genetic loss (green),
 - selection for scrapie without constraint, *i.e.* with maximum genetic loss (purple);
- **scrapie introduction:**
 - 1 initial infected ewe (dotted line),
 - 5 initial infected ewes (dashed line),
 - 1 infected ewe per year (plain line).

[1] A. D. Costard, Z. G. Vitezica, C. R. Moreno, and J.-M. Elsen. A dynamic deterministic model to optimize a multiple-trait selection scheme. *J. Anim. Sci.* 87(3): 885-894, 2009.

[2] S. Touzeau *et al.* Modelling the spread of scrapie in a sheep flock: evidence for increased transmission during lambing seasons. *Arch. Virol.* 151(4):735-751, 2006.