

HOST ADAPTATION IS CONTINGENT UPON THE INFECTION ROUTE TAKEN BY PATHOGENS

OUTLINE

- Pathogens can infect their hosts through different routes.
- Different infection routes trigger different physiological responses.
- How do distinct routes of infection shape adaptation to pathogens?

AIMS

- Compare the evolutionary response of a *D. melanogaster* population to bacterial infections, when infection happens via different routes.
- Determine correlated responses and tradeoffs between contrasting evolutionary scenarios.
- Determine correlated responses with different pathogens.

MAIN FINDINGS

- Markedly different evolutionary trajectories between the infection routes.
- No cross-resistance between alternate routes, indicating distinct genetic bases.
- Selected response to systemic infection is specific to the pathogen family.
 - Leads to a tradeoff in susceptibility to viral infections.
- Pathogen infection route differently affects host evolution.

METHODS

- Experimental Evolution of *Drosophila melanogaster* infected with *Pseudomonas entomophila* by two different routes (oral and systemic).
- Survival assays of control and selected lines after heterologous infections.
 - Bacteria— *P. entomophila*, *Pseudomonas putida*, *Serratia marcescens*, *Erwinia carotovora carotovora*, *Enterococcus faecalis*.
 - Viruses—*Drosophila C Virus* (DCV), *Flock House Virus* (FHV).

BASE POPULATIONS

- Outbred *D. melanogaster* population
 - 150 fertilized females caught in the wild in 2007
 - kept at high numbers in cages (>1000 individuals)
 - 3 week generation cycle.

SELECTION EXPERIMENT

- Replicate selection lines (n=4) were subjected to oral and systemic bacterial infection for >=25 generations with matched control line (Fig.1 and 2).
 - 600 individuals infected/generation.
 - Surviving individuals were used to start the next generation.
 - Oviposition at days 5-7 post infection.

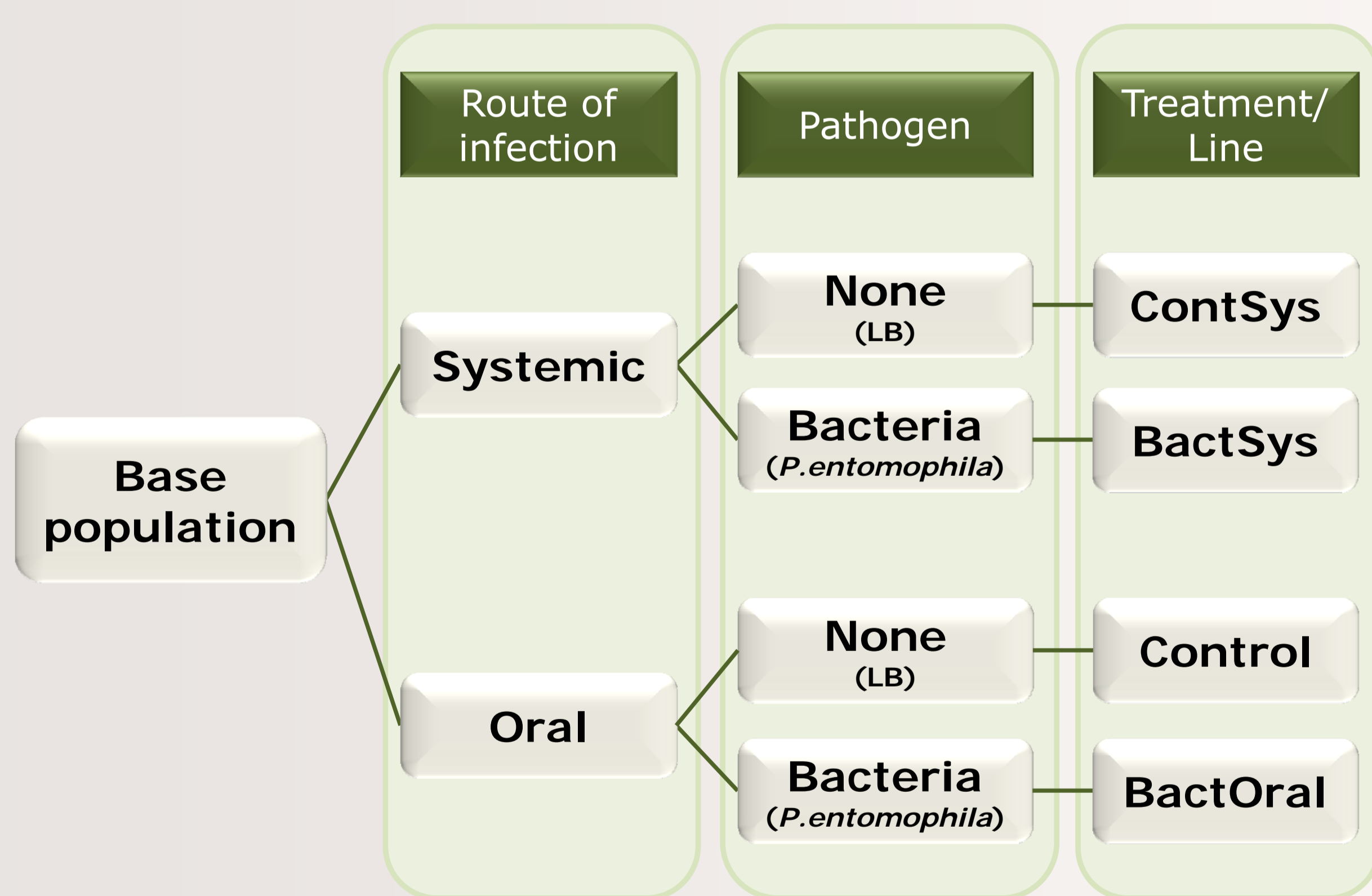


Figure 1—Outline of the selection treatments and corresponding selection lines.

CONCLUSIONS AND FUTURE PERSPECTIVES

- Adaptation is contingent upon the infection route taken by pathogens.
 - Different resistance mechanisms were selected by alternate routes of infection.
 - Unexpected high degree of specificity of the response in the BactSys lines.

Future prospects

- Determination of the targets of selection.
- Functional characterization of the selected mechanisms.

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DIFFERENT SELECTION DYNAMICS OF DIFFERENT ROUTES OF INFECTION

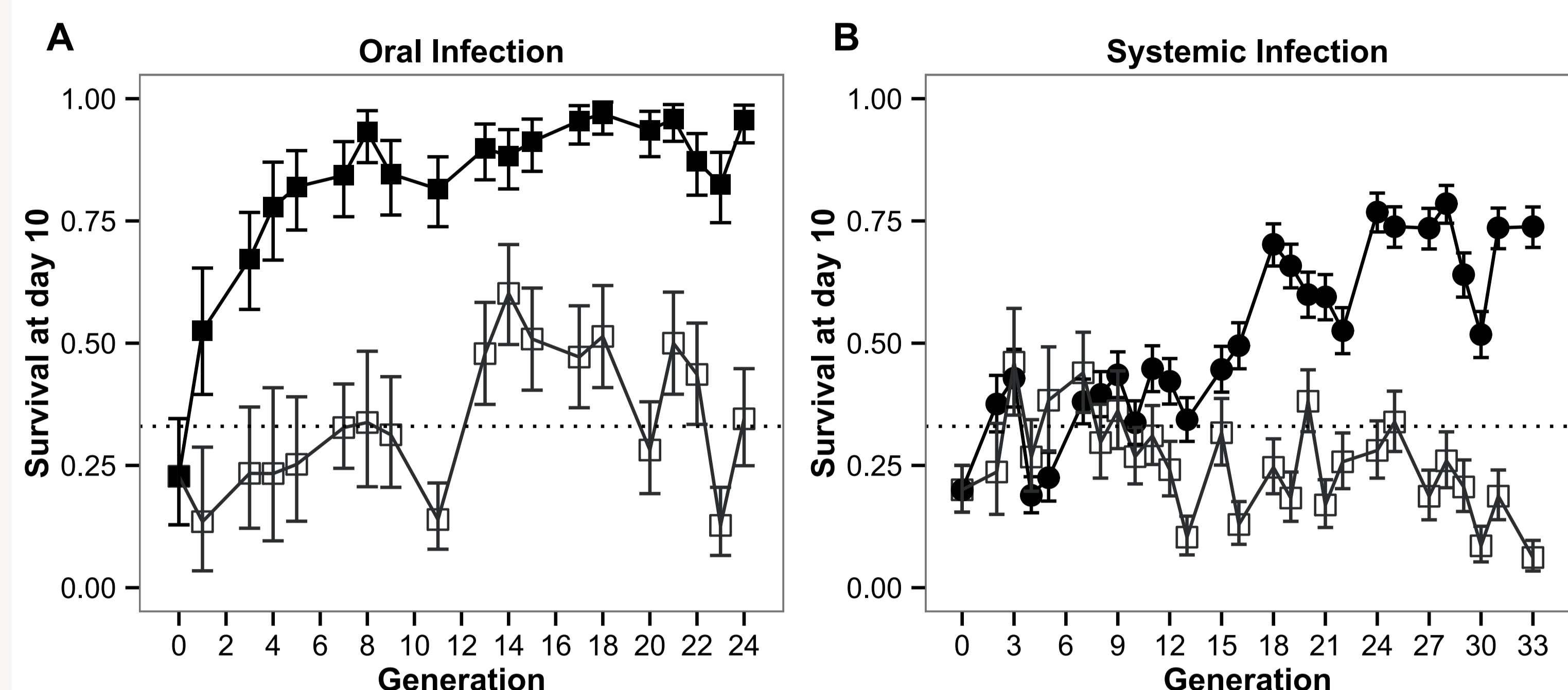


Figure 2—Mean (+/- 95%CI) survival of flies from the control and selected lines, ten days after infection with *P. entomophila*, across generations of selection. A—Survival of BactOral (■) and Control (□) lines after oral infection. B—Survival of BactSys (●) and Control (□) lines after systemic infection.

- Fast response (3-5 generations) of the BactOral lines.
 - Almost complete protection to infection.
- Slower (15-18 generations) response in the BactSys lines.
 - Lower plateau in the response.
- Differences in the genetic or environmental components of the variance may explain the observed selection dynamics.

SELECTED RESPONSES ARE SPECIFIC TO THE ROUTE OF INFECTION

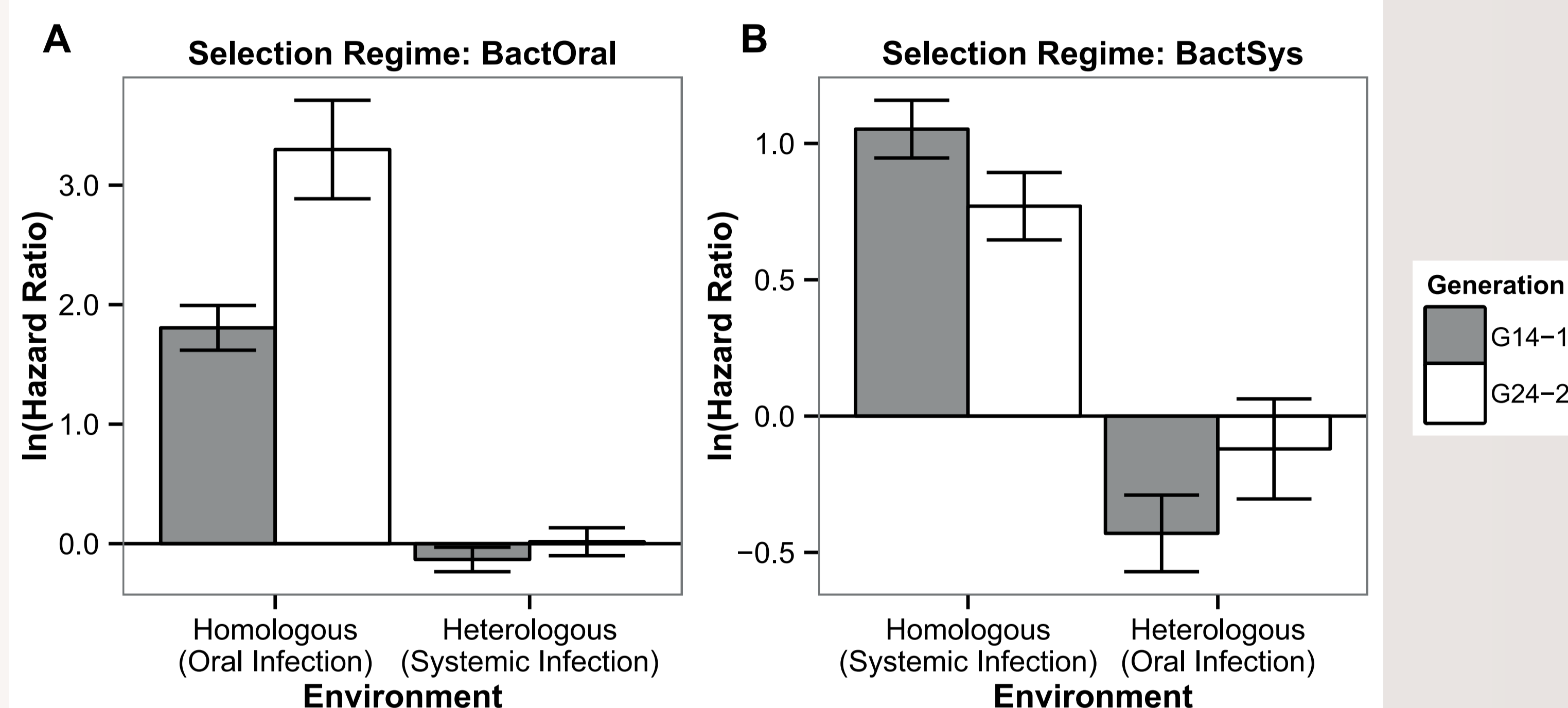


Figure 3—Mean loge hazard ratios (+/- 95% CI) between selected and matched control lines, at generations 15 and 25 of selection, after infection with *P. entomophila* A) Hazard ratio between BactOral and Control lines after oral (homologous) and systemic (heterologous) infection. B) Hazard ratio between BactSys and ContSys lines after systemic (homologous) and oral (heterologous) infection.

- Lack of cross resistance in heterologous infection scenarios.
- Distinct genetic basis for the selected resistance mechanisms in the two regimes.

SELECTED RESPONSE IS SPECIFIC TO THE PATHOGEN FAMILY

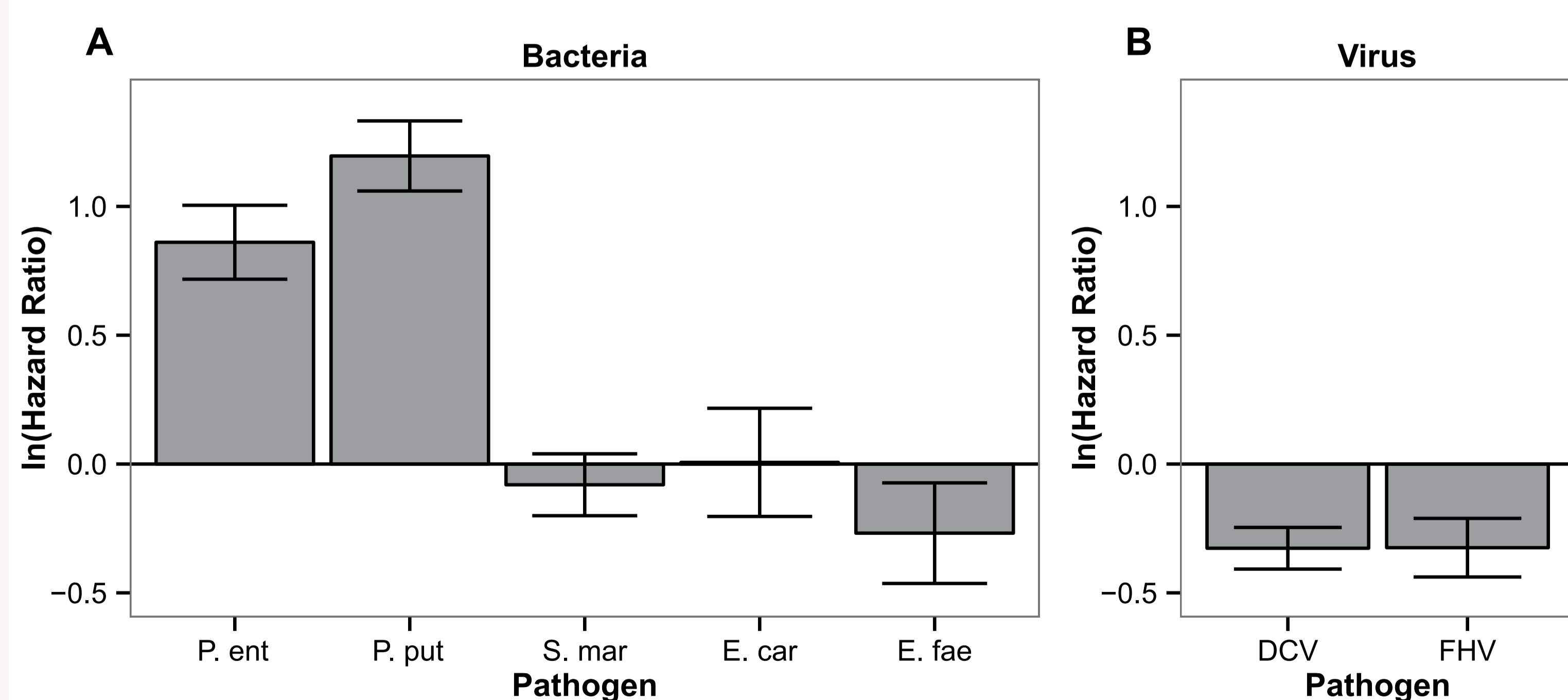


Figure 4—Mean loge hazard ratios (+/- 95% CI) between BactSys and ContSys lines (>27 generations of selection) after infection with A) the bacteria *P. entomophila*, *P. putida*, *S. marcescens*, *E. carotovora*, *E. faecalis* and B) *Drosophila C Virus* (DCV) and *Flock House Virus* (FHV).

- Increased resistance only to a closely related pathogen (*Pseudomonas putida*).
- Significantly lower resistance to viral infections.
- Selected response is specific to the pathogen family and leads to a significant tradeoff with resistance to viral pathogens.

REFERENCES

Y. H. Ye, S. F. Chenoweth, and E. a McGraw (2009) *PLoS pathogens*, vol. 5, no. 4, p. e1000385.
 Martins et al (*In press*) *PLoS Pathogens*, 10.1371/journal.ppat.1003601.