



Gene drives in the wild

Population genomics to inform development and translation of genetic biocontrols

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Wild ≠ Lab

Size & Morphology

Pathogens & Parasites

Life History

Litter size, generation time, senescence

Behaviour

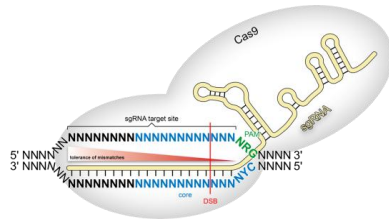
*Mate choice, dispersal,
territoriality/sociality*

Genetics

*Nucleotide variation, hybridisation,
genetic load*

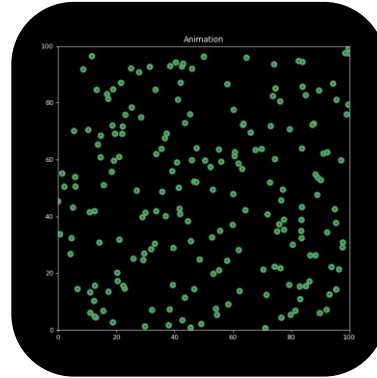


Population genomic analyses of pest populations are critical first steps



GD Design

- Identify CRISPR/Cas9 sgRNA target sites in suitable genes
- Scan for resistance alleles



GD Performance

- Evaluate population structure/gene flow
- Model drive efficacy, timelines, release strategies

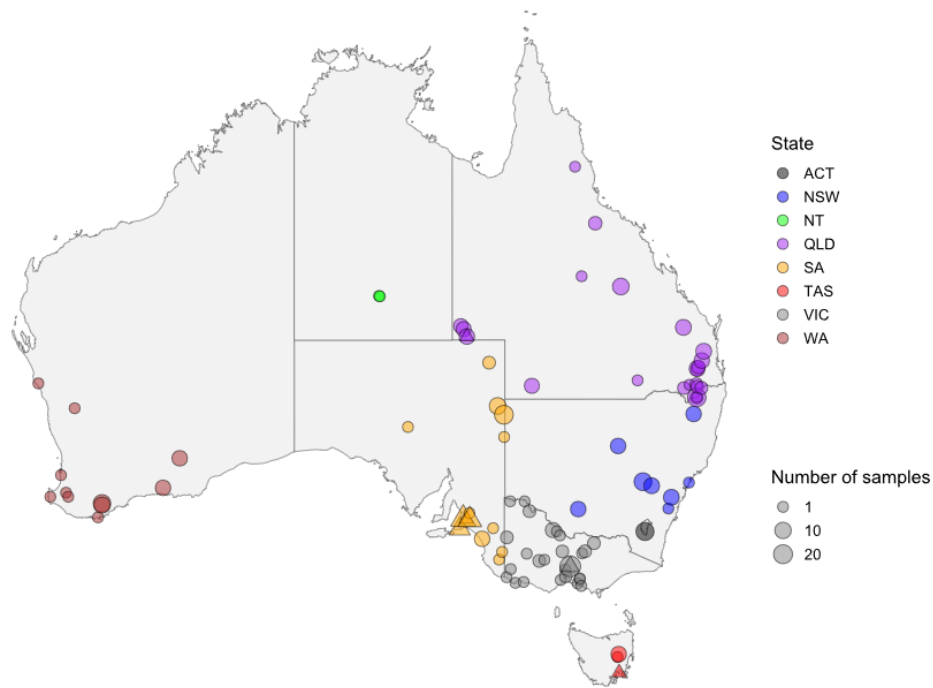


Risk and Governance

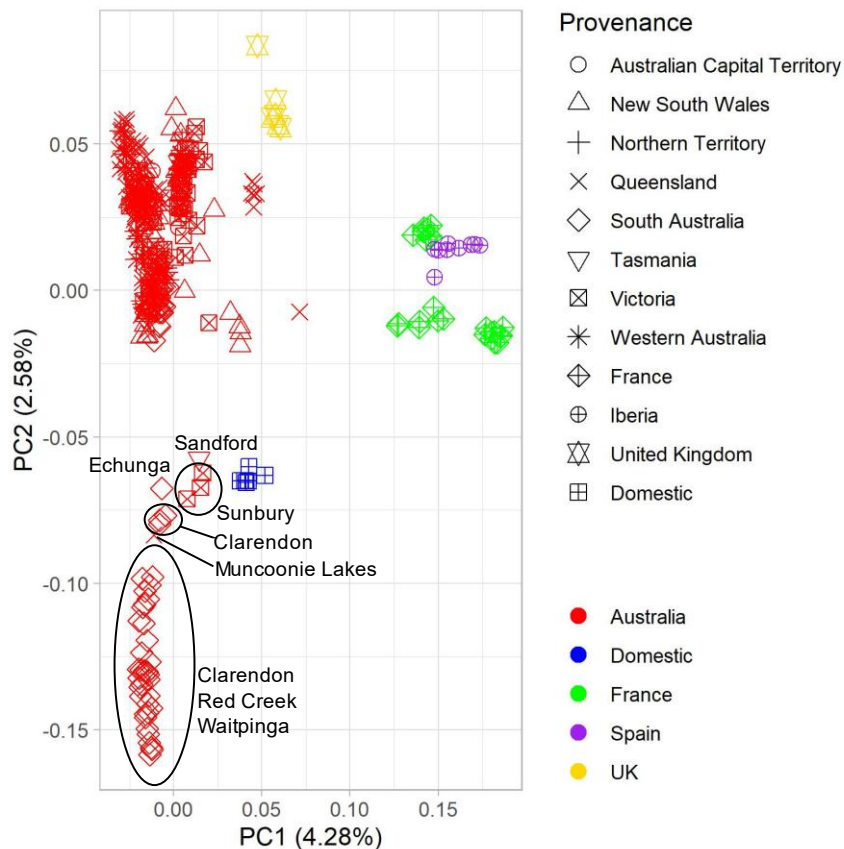
- Inform formal risk assessments
- Fulfill regulatory obligations

Population genomics of invasive rabbits: Methods

- Extracted DNA from **522** rabbits sampled across Australia, Europe, and domestic breeds
- Performed whole-genome sequencing (Illumina NovaSeq S4)
- Bioinformatic processing resulted in final sequence dataset including 402 genomes:
 - Australia (N=**356**)
 - Europe (N=**40**)
 - Domestic (N=**6**)
- Identified single nucleotide polymorphisms (SNPs) across genome

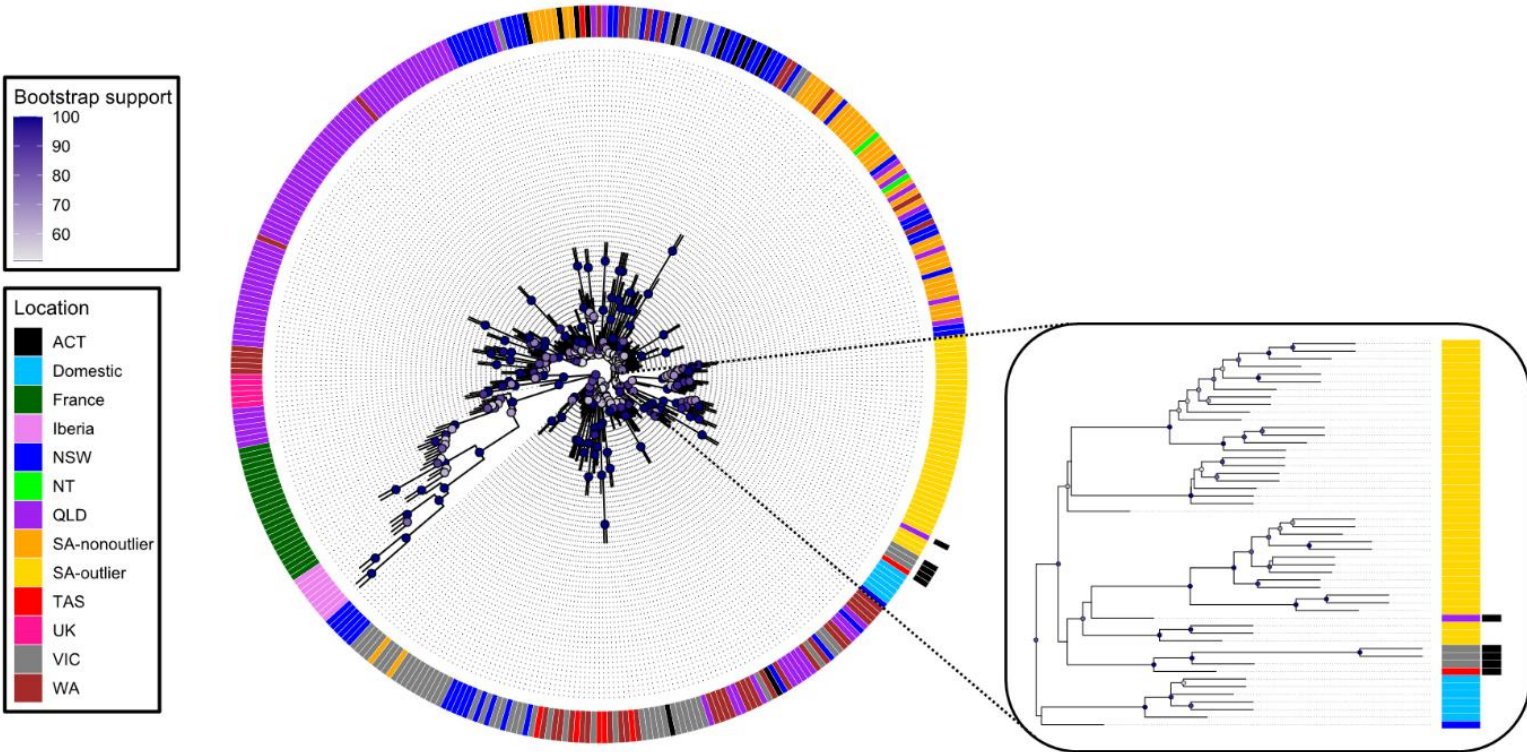


Population genetic structure in rabbits: Australia & Europe



- Little apparent genetic structure within Australia
 - Pairwise genetic differentiation (F_{st}) uniformly low among Australian locales
- Most Australian rabbits closely clustered with UK rabbits
- Detected outliers in SA that appeared more similar to domestic rabbits

Nuclear phylogeny supported domestic origins of outliers

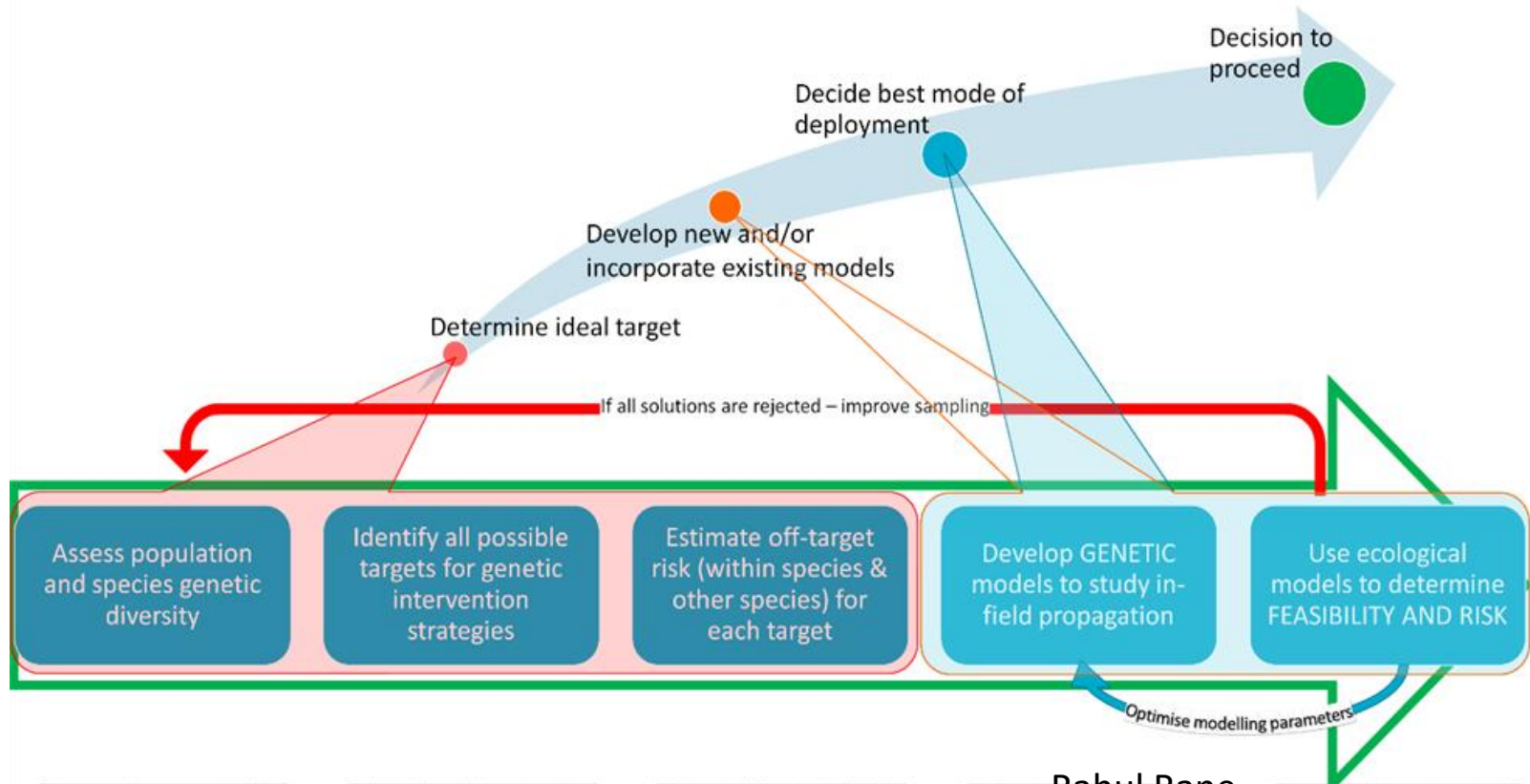


Summary

1. Australian rabbits are well-differentiated from European populations, but relatively homogeneous overall with no strong evidence of population genetic structure within Australia.
2. Suggests high gene flow, common source of introduction (UK)
3. Previously undescribed outlier population in SA, likely due in part to domestic introgression(?)

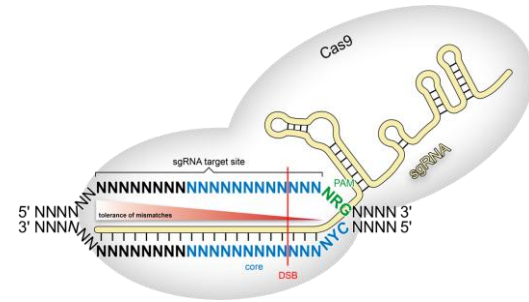


Gene drive Utility And Risk Determination (GUARD)

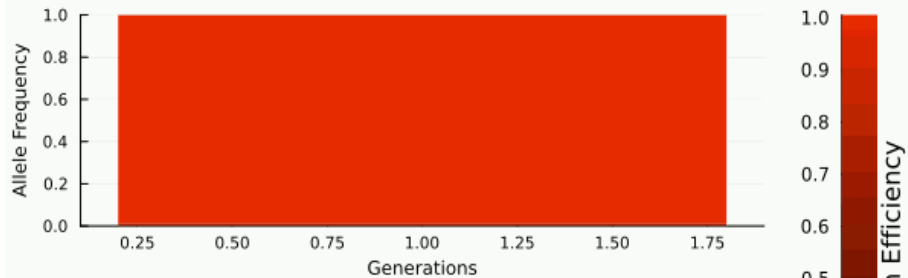


Finding suitable candidates

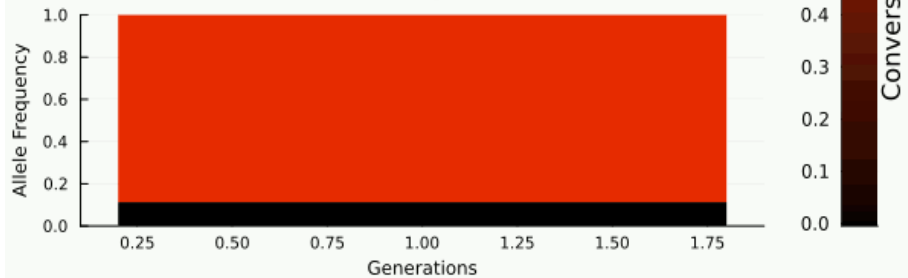
- Located 106,177 suitable sequences
- 2158 of those are within 1302 genes
- Preliminary assessment found two genes could be of interest



Australia



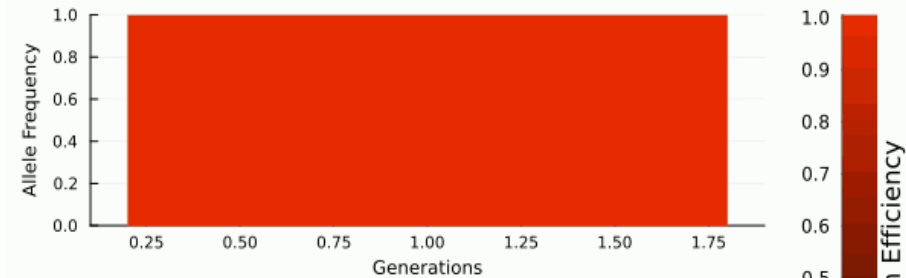
Europe



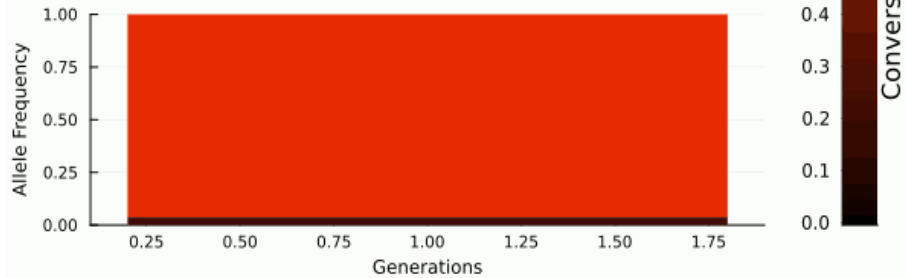
Presence of resistance and strong
gene flow

Reincursion with resistance

Australia



Europe



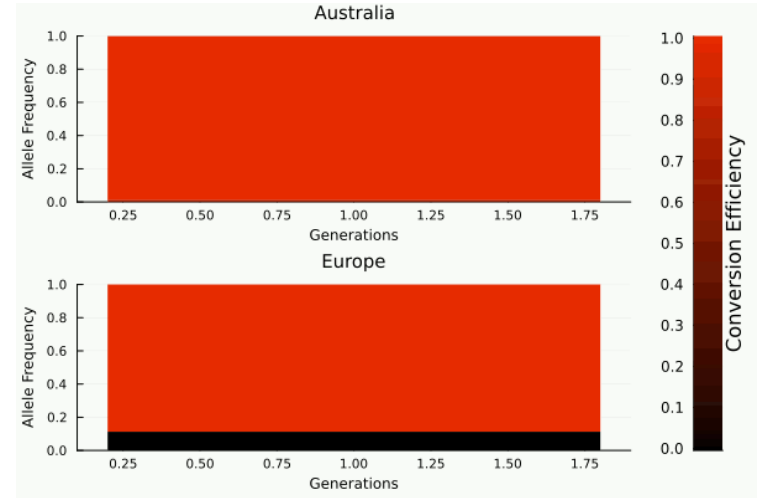
Partial to no resistance and strong
gene flow

Gene drive spreading everywhere !!!

Blue = Gene drive haplotype (Sex-biasing)
Red = Wild type susceptible to gene drive
Black = Wild type resistant to gene drive

Challenges

- Logistics/Practicality
- Fine-tuning the gene drive effects
- Upscaling – deployment strategies
- Risks
 - Reintroduction
 - Effects on non-target population
 - Ecological
 - Socio-economic



Summary (2)

1. There are many potential candidates identified bioinformatically, further work required to understand which genes are most suitable
2. What gene drive options will be possible? Proof of concepts required
3. Considerations (regulatory/ethical) required into what are acceptable impacts of gene drive



CSIRO

Thank you

Tanja Strive

Ina Smith

Ángel David Popa-Baez

Maria Jenckel

Sarah Topfer

GUARD

Rahul Rane

Benjamin Camm

Luke Vincent

Alexandre Fournier-Level

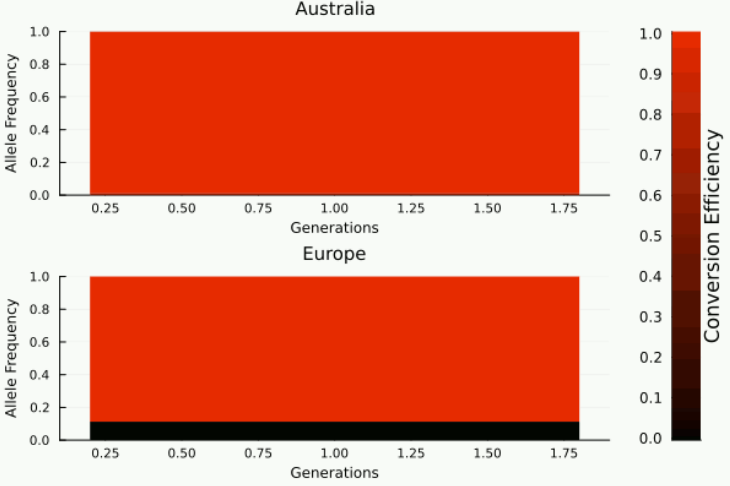
Owain Edwards



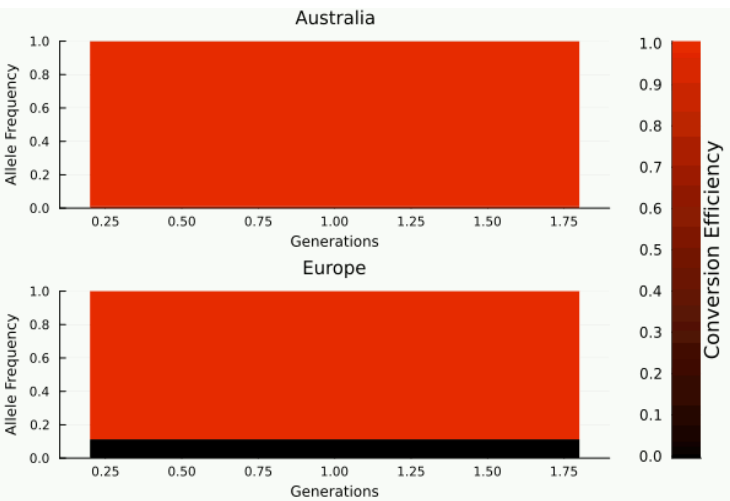
Many collaborators who contributed samples!



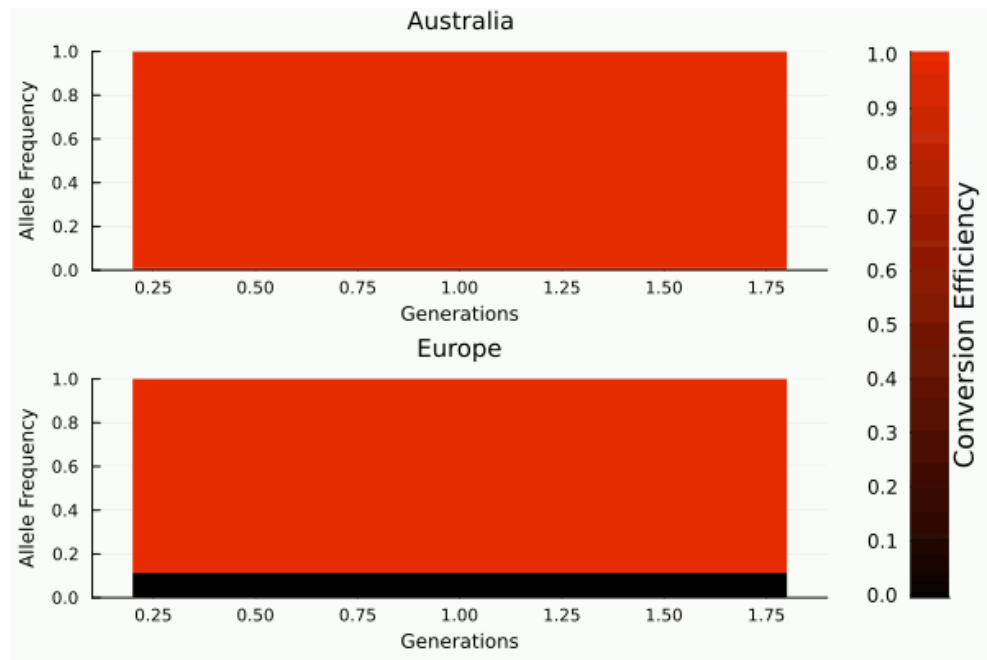
Braidwood, NSW



Low migration rate, equal population size



High migration rate, equal population size



Low migration rate, low European population size

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