Introgression of a block of genome with many weakly selected variants

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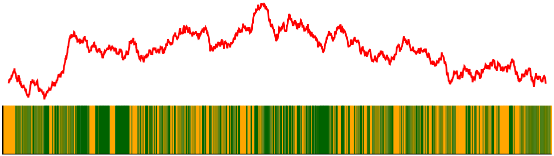
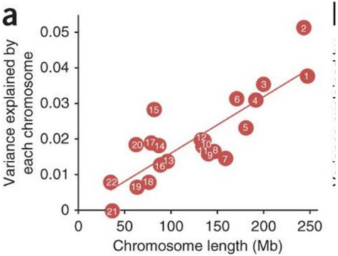
IST Austria



Sachdeva and Barton, *Introgression of a block of genome under infinitesimal selection*, Genetics (2018).

Sachdeva and Barton, *Replicability of introgression under linked, polygenic selection*, Genetics (2018).

Most traits are *highly* polygenic

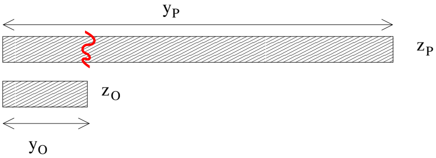


From: Yang et al, Nature Rev Genet, 2011

- $\mathcal{O}(10^5)$ common SNPs→ causal effects on height. [Boyle et al, 2017]
- infinitesimal model *with linkage*.

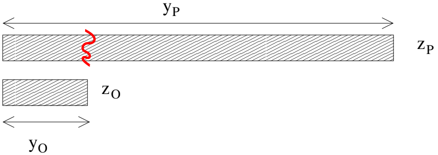
Infinitesimal model *with linkage*

Inheritance of **blocks** of genome:



Infinitesimal model *with linkage*

Inheritance of **blocks** of genome:

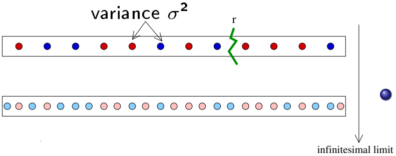


$$P(z_O) = \mathcal{N}\left[\frac{y_O}{y_P} z_P, V_0 y_O \left(1 - \frac{y_O}{y_P}\right)\right].$$

[Robertson, 1977]

$V_0 \approx$ **heterogeneity** along the genome.

Approaching the infinitesimal limit

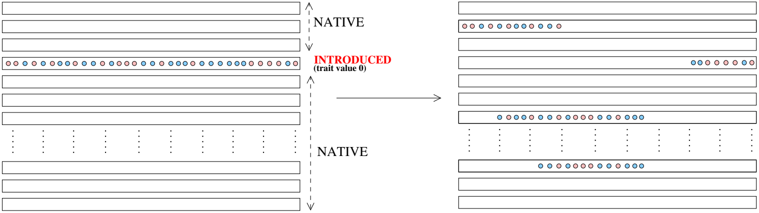


- L loci (uncorrelated effects) spread uniformly.

$$\boxed{V_0 = \sigma^2/r \rightarrow \text{genic variance per unit map length}}$$

When can selection ‘see’ discrete loci?

Spread of a genome with linked, weakly selected variants



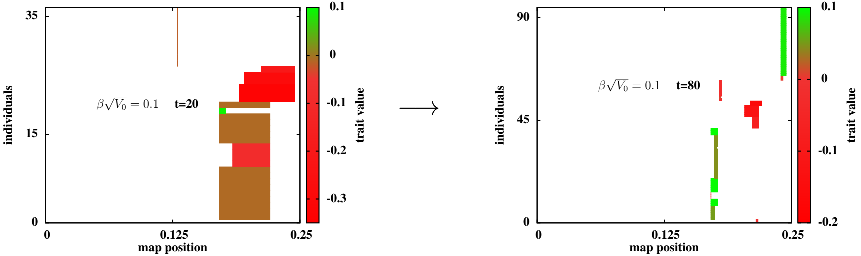
fitness $\propto e^{\beta z}$

NO new mutations

- Introgression due to **weakly selected, linked** loci vs. **neutral** introgression?
- What determines 'success' of different fragments of a block?

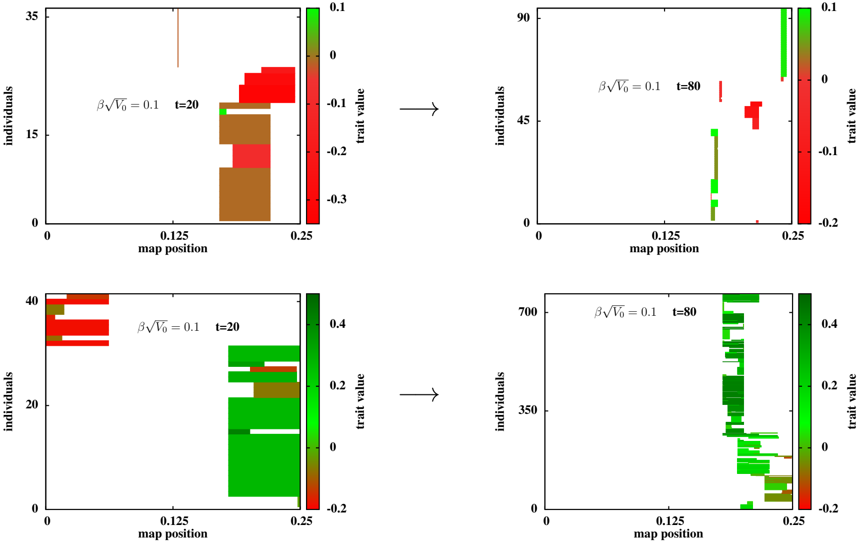
Initial spread of introduced genome: snapshots

Model as a *branching process*: at most **1** introduced fragment per individual

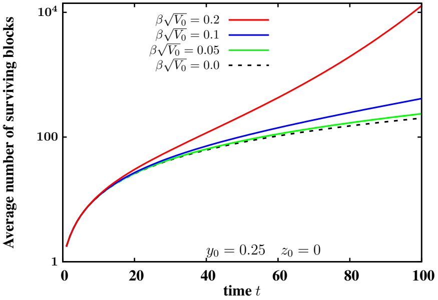


Initial spread of introduced genome: snapshots

Model as a *branching process*: at most **1** introduced fragment per individual



Rate of introgression



Exponentially fast vs. $\sim t$ spread

Weakly selected variants $\overset{?}{\approx}$ neutral variants?

Not if linked

Medium-sized fragments drive exponential introgression

Fragment with map length y_* and trait value z_*:

- Typical $z_* \sim \pm\sqrt{V_0 y_*}$, assuming uncorrelated loci.
- $\beta z_* > y_* \implies$ **successful fragment** that increases *intact* exponentially.
- Successful fragments: *typical* map length and growth rate $\propto \beta^2 V_0$.

β → strength of selection on trait; $V_0 = \sigma^2/r$ → variance per unit map length

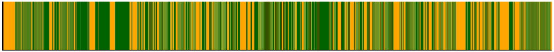
Introgression of individual variants: initial vs. long-term

80 copies of $40cM$ block with 2048 loci ($\beta\sigma = 0.0007$) introduced into population ($N = 4000$).

Analytical solution for short-term dynamics

$\downarrow$

Expected growth rate of variant $\approx \beta z - y$ for fastest-growing *containing* fragment.



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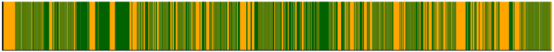
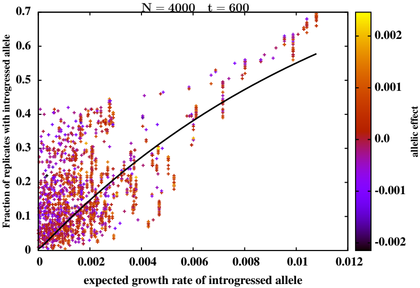
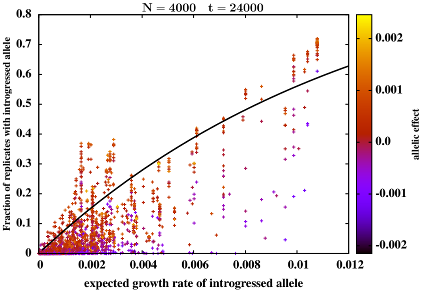
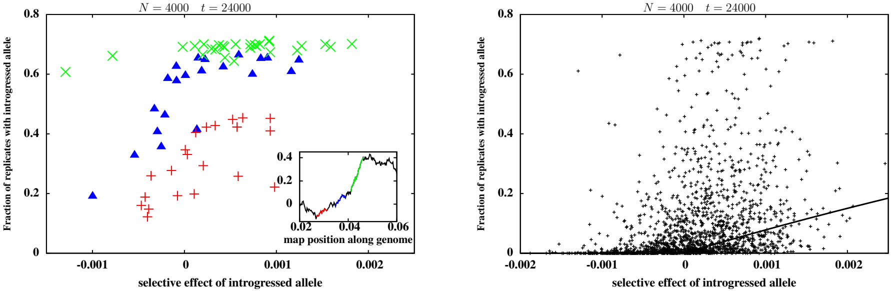






Long-term introgression: role of individual effects



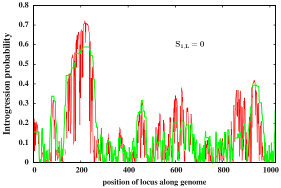
Own effect → **fine-scale variation** at long times in large populations.

Conclusions

- **Linked variants** crucial to polygenic adaptation.
- **Exponential spread** of genetic material even under infinitesimal selection.
- Successful fragments are **medium-sized**.
- **Two phases** of introgression: short-term (hitchhiking with single successful fragments) vs. long-term (partial purging of deleterious variants).
- Individual variants with high introgression probability **may not be adaptive**.

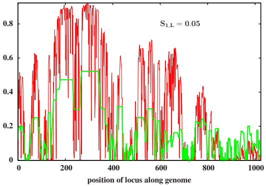
Understanding heterogeneous genomic landscapes

Neutral



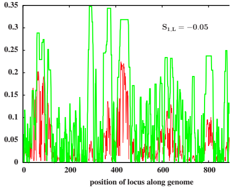
A

Beneficial



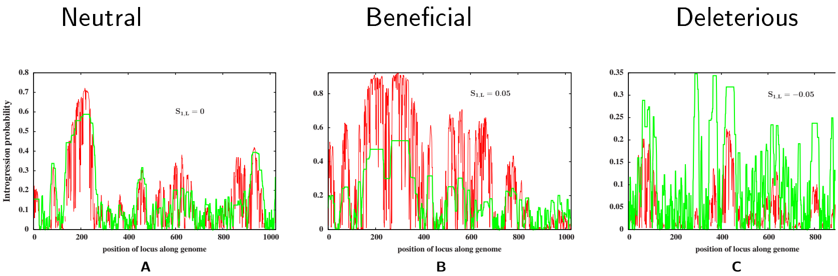
B

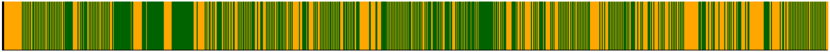
Deleterious



C

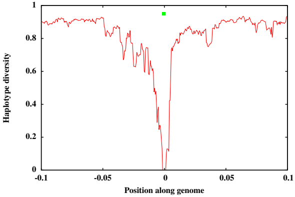
Understanding heterogeneous genomic landscapes

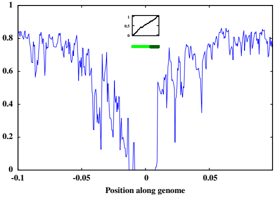


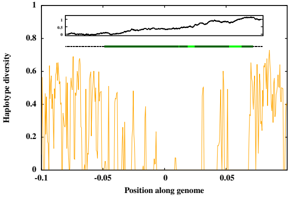


2-tiered description: Weak pairwise associations between linkage blocks?

Sweep signatures: one vs. multiple adaptive variants?







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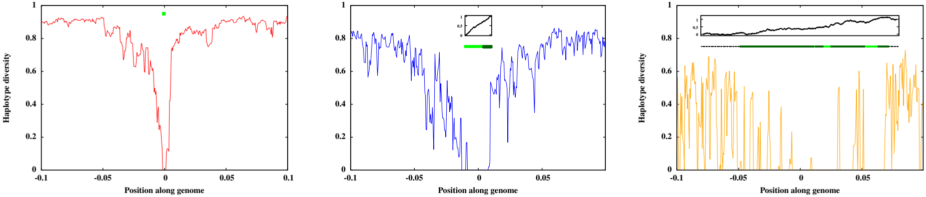
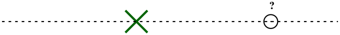


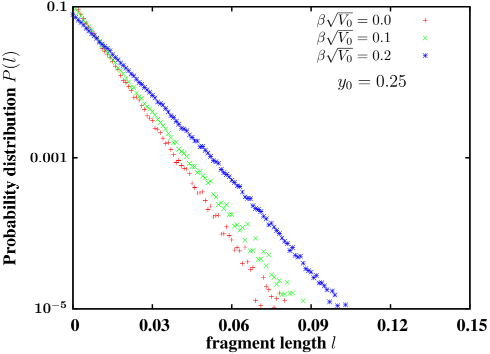


vs.

Response from standing variation

- Spread of a single genome into a heterogeneous population?
- When does selection see discrete loci?
- Heterogeneity along the genome in the infinitesimal limit?

Wide distribution of fragment lengths

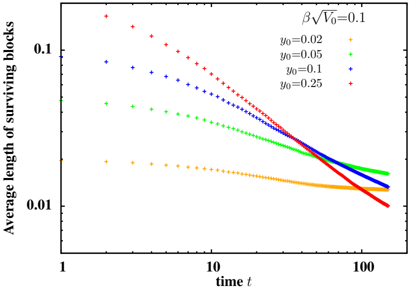


$t = 100$ generations after the introduction event.

Introgression of a *beneficial* block

Long vs. short introduced blocks

Average length of surviving fragments.



Medium-sized blocks have longest descendant fragments.

To be a long block or not to be?

Depends on the initial advantage of the block.