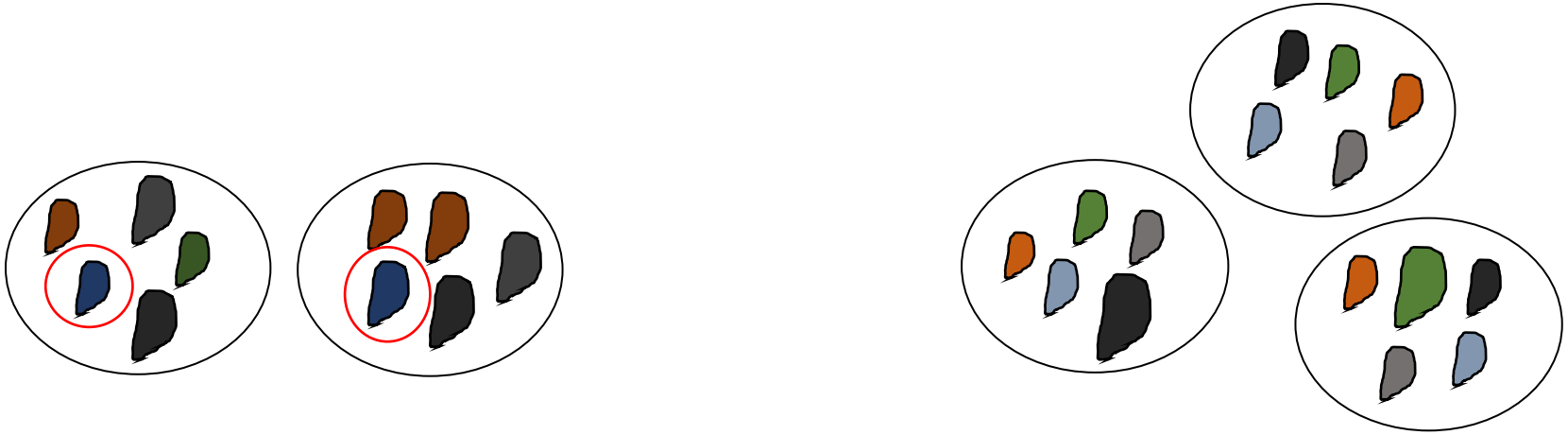
GENETIC DIVERSITY AND GENETIC DIFFERENTIATION



GENETIC MARKERS?

- mitochondrial DNA (16S, COI)
- allozymes (protein isozymes)
- microsatellites (repeatable tandems, e.g. $(ACA)_n$)
- AFLP (DNA fragments obtained by enzymatic digestion)
- SNPs (single nucleotide polymorphisms: A/C, G/T, A/C…)
- mRNA (transcriptomics)

GENETIC MARKERS?

- mutation rate (mtDNA low, microsatellites and SNPs high)
- neutral or ambiguous or putatively under selection
- cost – money and time, **KNOWLEDGE AND SKILLS**
- number – genome wide (SNPs) or localised insights, statistical power
- development of new markers and specificity

GENETIC DIVERSITY

- number or genetic variants in population (allelic richness- number of alleles in population, nucleotide diversity)
- heterozygosity (AA, AB, BB)
- private alleles – alleles present in only particular population

GENETIC DIVERSITY - IMPORTANCE

Adaptation – genom-wide diversity enables variability for selection to act upon in changed environmental conditions) – its main prerequisite for adaptive evolution

Inbreeding depression- decreased fitness due to reproduction of related individuals- it's a consequence of low genetic diversity and **mutation load** – number of detrimental alleles in population

For maintenance of genetic diversity population size and gene flow are of paramount importance


Green bridges – facilitate gene flow in fragmentated ecosystems

Inbreeding depression is the reduced survival and fertility of offspring of related individuals. Large effects are documented in wild animal and plant populations, as well as in humans.

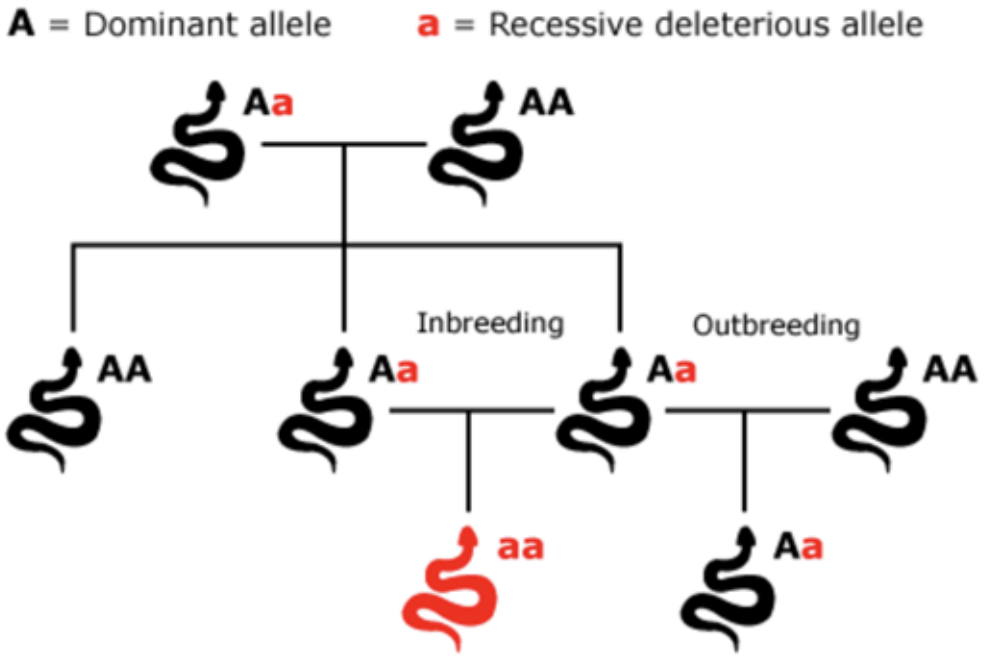
1) Presence of (largely recessive) **deleterious mutations** that are present at low frequencies in populations (so that inbreeding increases the frequency of individuals expressing their effects; the ***'dominance hypothesis***') (AA, Aa, aa)

1) Inbreeding **decreases number of heterozygotes** for the traits under balancing selection (here, homozygotes would have lower fitness; the ***'overdominance hypothesis***') (AA, Aa, aa)

Inbreeding decreases **standing genetic variation** in population and thus **diminishes adaptive capacity**

- 40 adders (*Vipera berus*, shown at right) experienced inbreeding depression when farming activities in Sweden isolated them from other adder populations.
- Higher proportions of stillborn and deformed offspring were born in the isolated population than in the larger populations (31.6%).
- When researchers introduced in 1992 twenty male adders from other populations — an example of **outbreedin**g — the isolated population recovered and produced a higher proportion of viable offspring.
- Lack of unviable offspring is explained by intra uterine selection of sperm containing optimal haplotypes (cryptic female choice)





Genetic rescue!

- 10.1016/j.cub.2020.08.059

The Linnean Society BIOLOGICAL Journal of the Linnean Society

Biological Journal of the Linnean Society, 2015, **114**, 474–483. With 2 figures

Darwin was right: inbreeding depression on male fertility in the Darwin family

GONZALO ÁLVAREZ[1], FRANCISCO C. CEBALLOS*[1] and TIM M. BERRA FLS[2,3]

Analysis of the number of children per woman through zero- inflated regression models showed a ***significantly adverse effect of the husband inbreeding coefficient on family size***

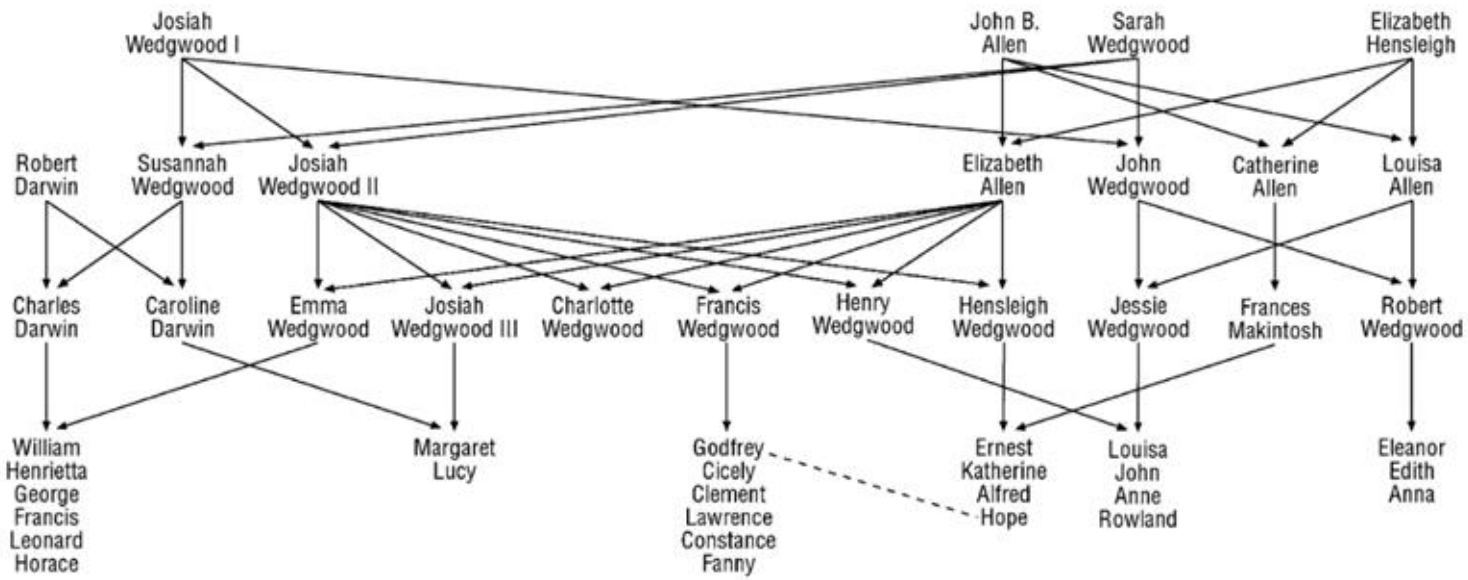


Figure 1. Partial pedigree of the 26 individuals of the Darwin–Wedgwood dynasty considered for the fertility analysis.

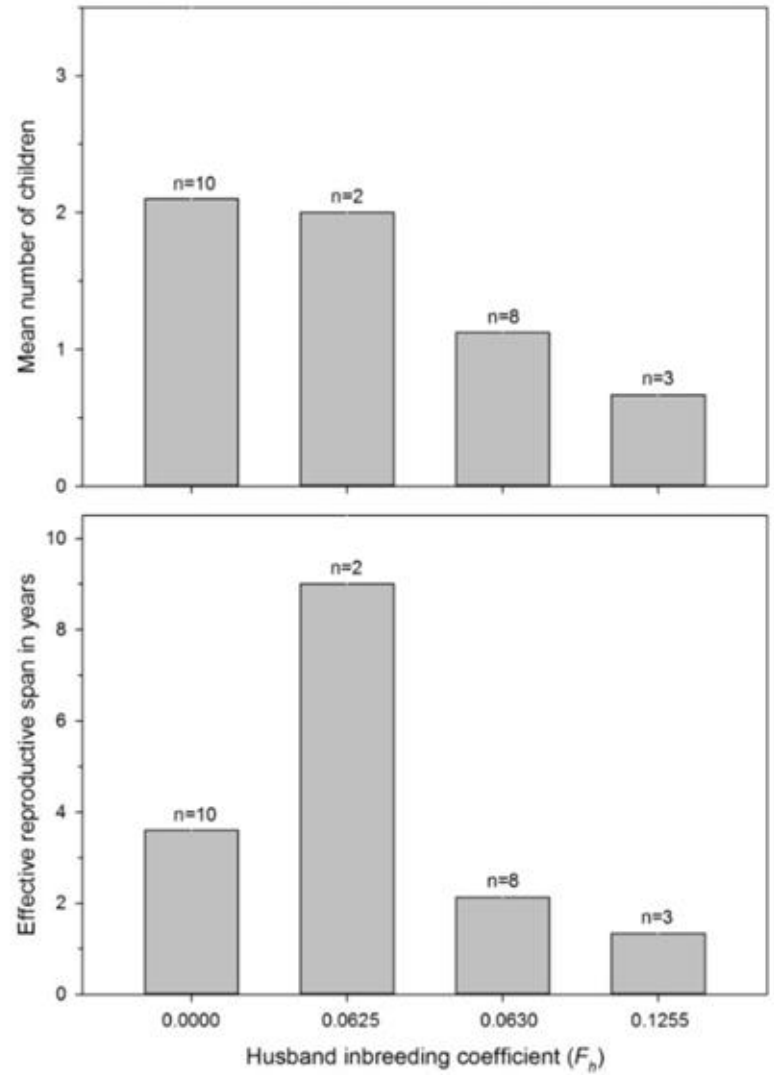
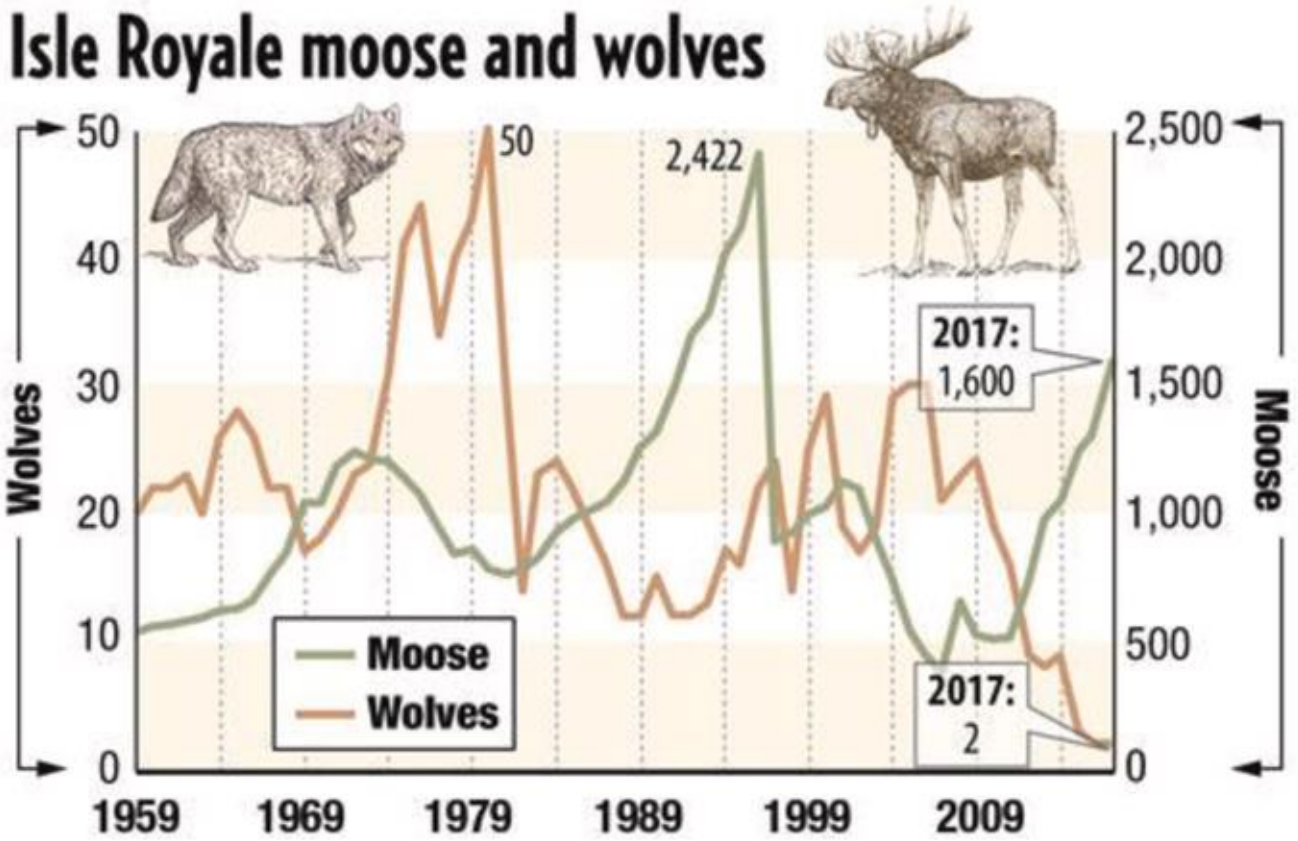


Figure 2. Mean number of children and effective reproductive span for different values of husband inbreeding coefficient (F_h) from 23 Darwin–Wedgwood marriages. The bars corresponding to $F_h = 0.0630$ represent fertility values for Charles Darwin's son.

- The Isle Royale population was founded about 1950 by wolves from the mainland population
- In 1980. **virus was introduced** in population by visitor s dog
- A **male wolf** known as M93 migrated from nearby mainland Ontario, Canada in 1997 .
- Behaviourally dominant over resident wolves, he reproduces with majority of females and their descendants quickly dominated the genetic ancestry of the population. By 2008, **59.4 % of the genetic ancestry** in the population was from him (inbreeding coefficient droping from 0.81 down to 0.09).



- The population numbers of Isle Royale wolves have declined and in 2012 and 2013, there were only 9 and 8 wolves, respectively, the lowest numbers ever recorded.

- In 2017. only 2 wolfs recorded - wolfs were then introduced from a nearby island
- Only wolfs introduced from the islet survived

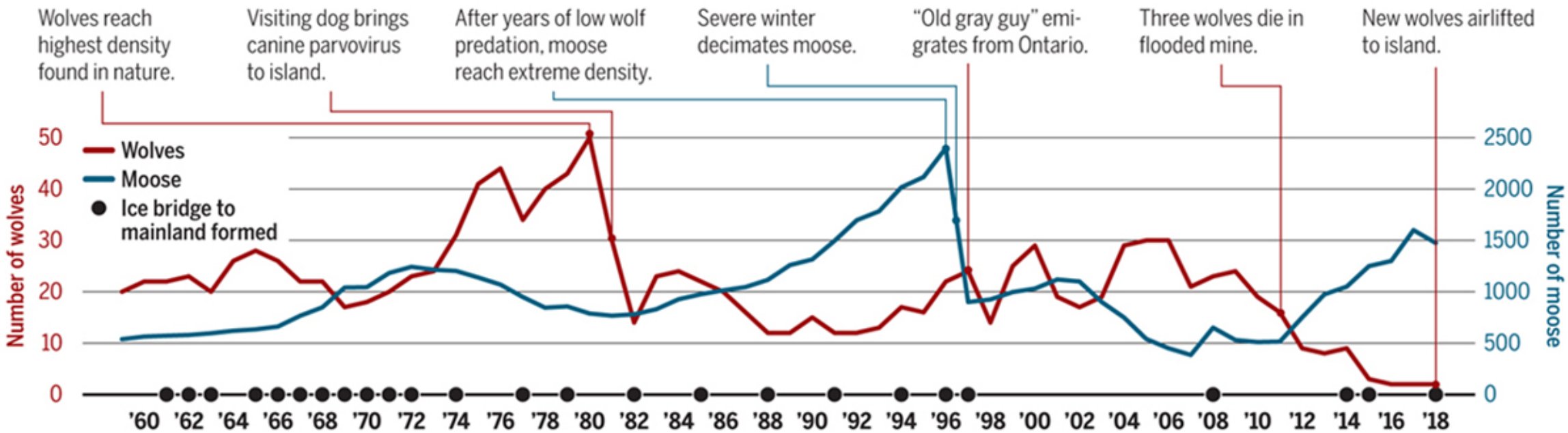


„A 2009 paper in *Biological Conservation* reported that 58% of examined wolves had congenital spinal deformities, compared with only 1% of wolves in other populations. ”

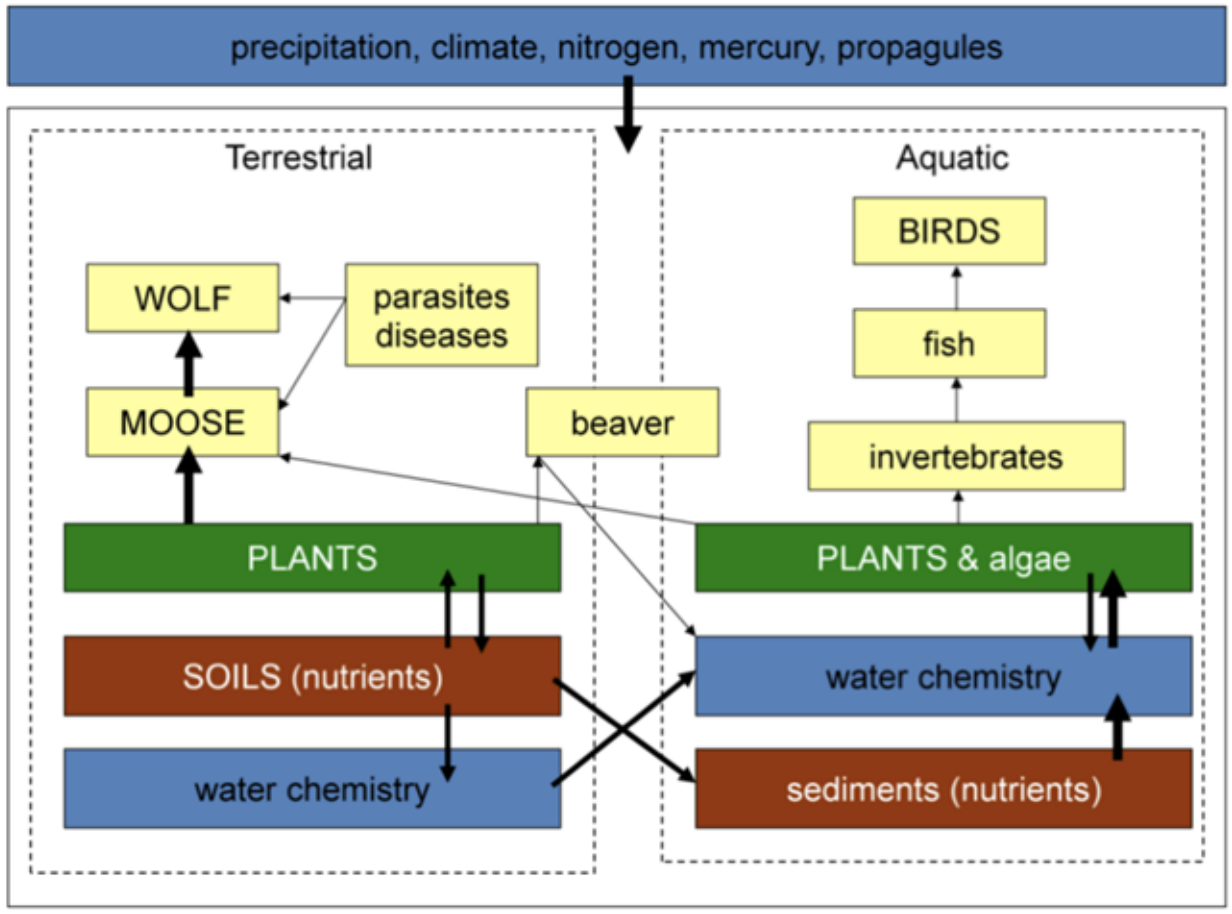
wolf and moose dynamic

A dance of predators and their prey

The Isle Royale study shows the importance of chance events as well as climate change, as ice bridges that allow immigration by mainland wolves are now rare.



To introduce or not to introduce?



Trophic web and resource cycle for Isle Royale (Figure 3 from Schlesinger et al. 2009).



Not genetic rescue, but genetic replacement!

SCIENCE ADVANCES | RESEARCH ARTICLE

EVOLUTIONARY BIOLOGY

increased homosigosity of deleterious mutations

Genomic signatures of extensive inbreeding in Isle Royale wolves, a population on the threshold of extinction

Jacqueline A. Robinson[1*†], Jannikke Räikkönen[2], Leah M. Vucetich[3], John A. Vucetich[3], Rolf O. Peterson[3], Kirk E. Lohmueller[1,4,5‡], Robert K. Wayne[1‡]

The observation that small isolated populations often suffer reduced fitness from inbreeding depression has guided conservation theory and practice for decades. However, investigating the genome-wide dynamics associated with inbreeding depression in natural populations is only now feasible with relatively inexpensive sequencing technology and annotated reference genomes. To characterize the genome-wide effects of intense inbreeding and isolation, we performed whole-genome sequencing and morphological analysis of an iconic inbred population, the gray wolves (*Canis lupus*) of Isle Royale. Through population genetic simulations and comparison with wolf genomes from a variety of demographic histories, we find evidence that severe inbreeding depression in this population is due to increased homozygosity of strongly deleterious recessive mutations. Our results have particular relevance in light of the recent translocation of wolves from the mainland to Isle Royale, as well as broader implications for management of genetic variation in the fragmented landscape of the modern world.

Genetic drift

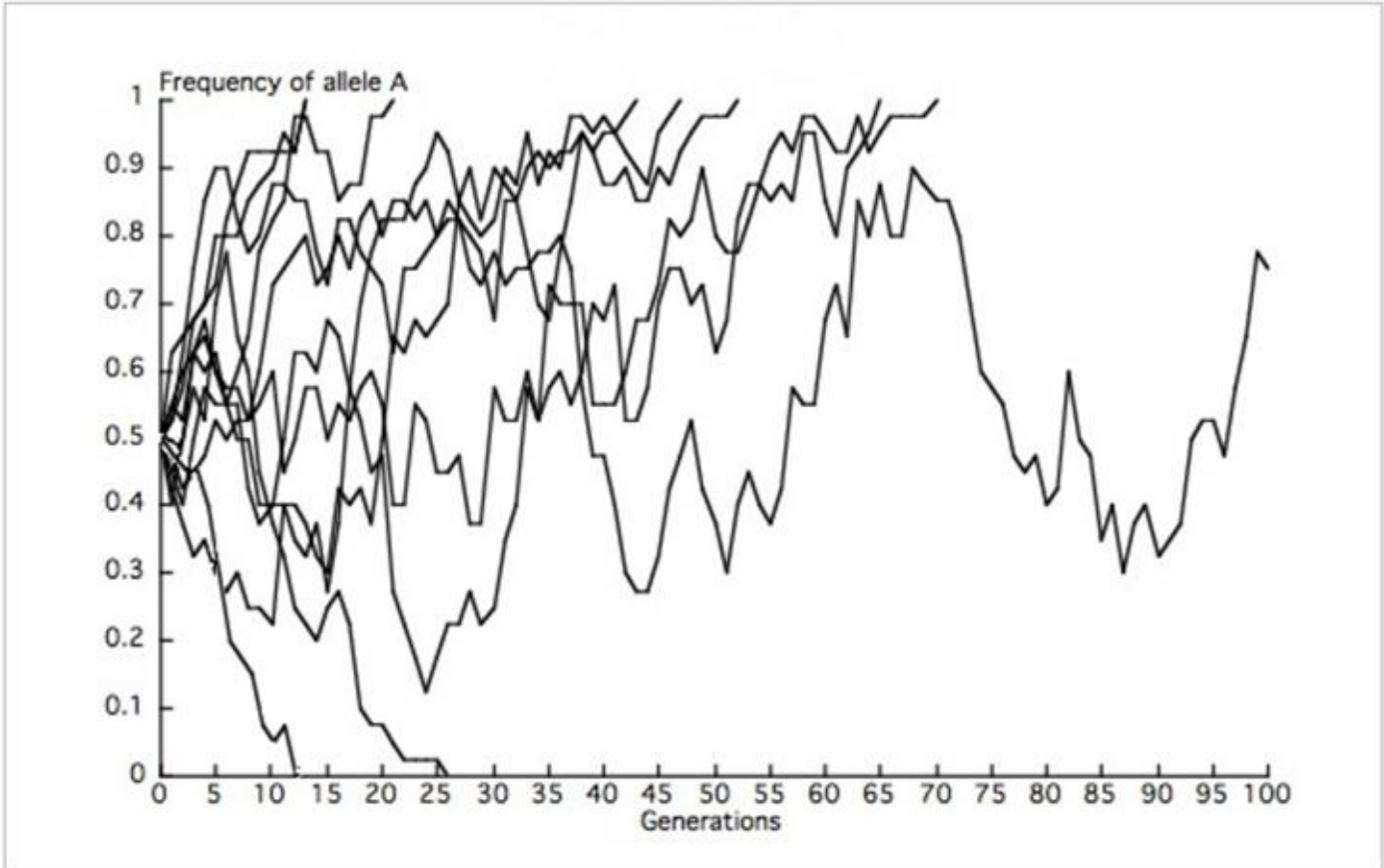


Figure 2: Simulations of allele-frequency change in 10 replicate populations (N = 20)
Since the initial frequency of the A allele = 0.5, we expect A to be fixed in 5 populations and lost in 5 populations, but our observations deviate from expectations because of the finite number of populations. In this run of simulations, we see 7 instances of fixation (p = 1), 2 instances of loss (p = 0), and one instance in which there are still two alleles after 100 generations. In this last population, A would eventually reach fixation or loss.
© 2010 Nature Education All rights reserved.

GENOMIC DIFFERENTIATION

GENOMICS - NGS

RAD TAGS

DAAN	ACTGGCAGCGAATCTAGTGCGTAA
LOTTE	ACTGGCCGCGAATCTAGTGCGTAA
LEVI	ACTGGCCGCGAATCTAGTGCGTAA
LISA	ACTGGCAGCGAATCTAGTGCGTAA
EMMA	ACTGGCCGCGAATCTAGTGCGTAA
SEM	ACTGGCAGCGAATCTAGTGCGTAA

SNPs

- ≈ *towsends SNPs per individual*

GENOMICS - NGS

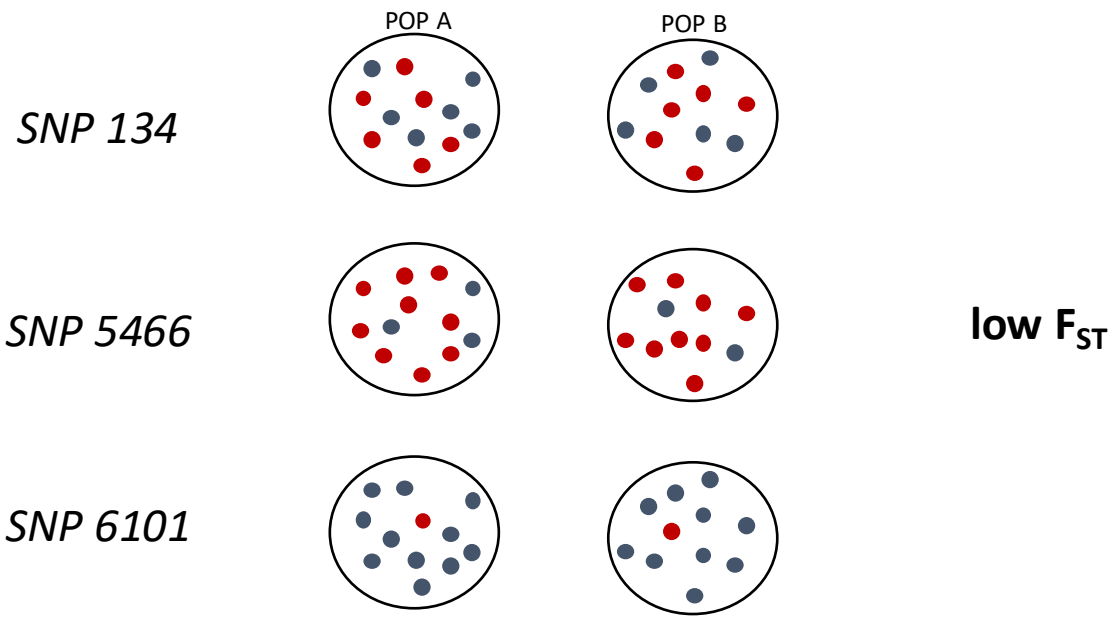
RAD TAGS

DAAN	ACTGGCAGCGAATCTAGTGCGTAA
LOTTE	ACTGGCCGCGAATCTAGTGCGTAA
LEVI	ACTGGCCGCGAATCTAGTGCGTAA
LISA	ACTGGCAGCGAATCTAGTGCGTAA
EMMA	ACTGGCCGCGAATCTAGTGCGTAA
SEM	ACTGGCAGCGAATCTAGTGCGTAA

SNPs

- ≈ *towsends SNPs per individual*

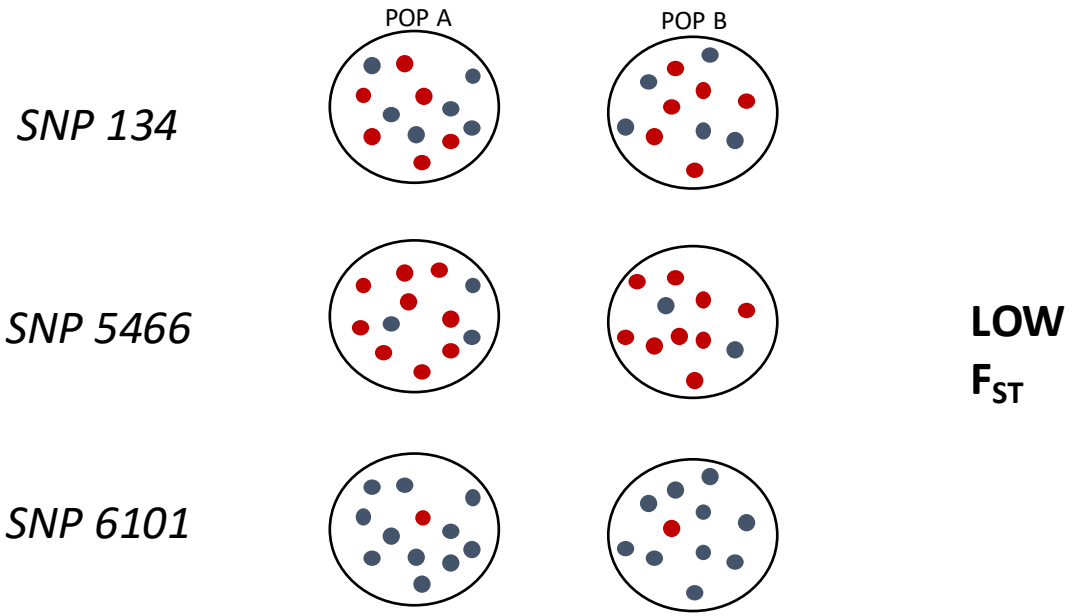
LOCUS F_{ST}

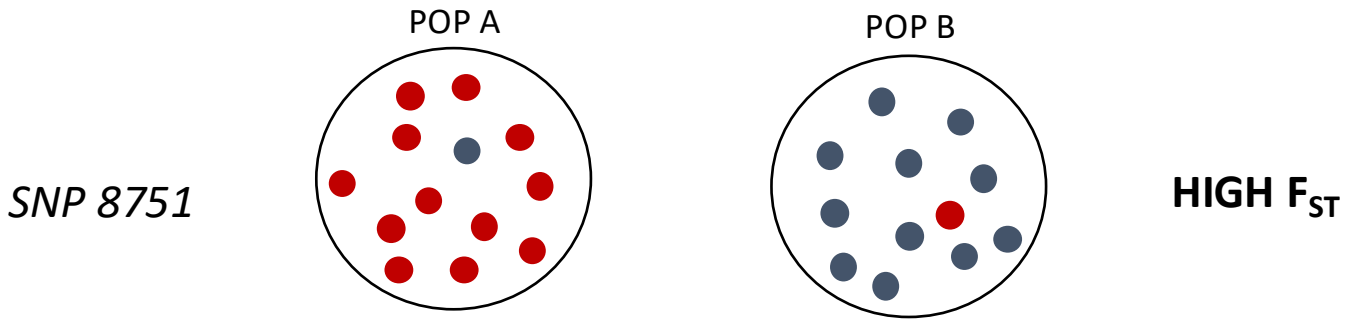


low F_{ST}

F_{ST} is fixation indeks, comparison of genetic variability between populations with genetic variability within populations

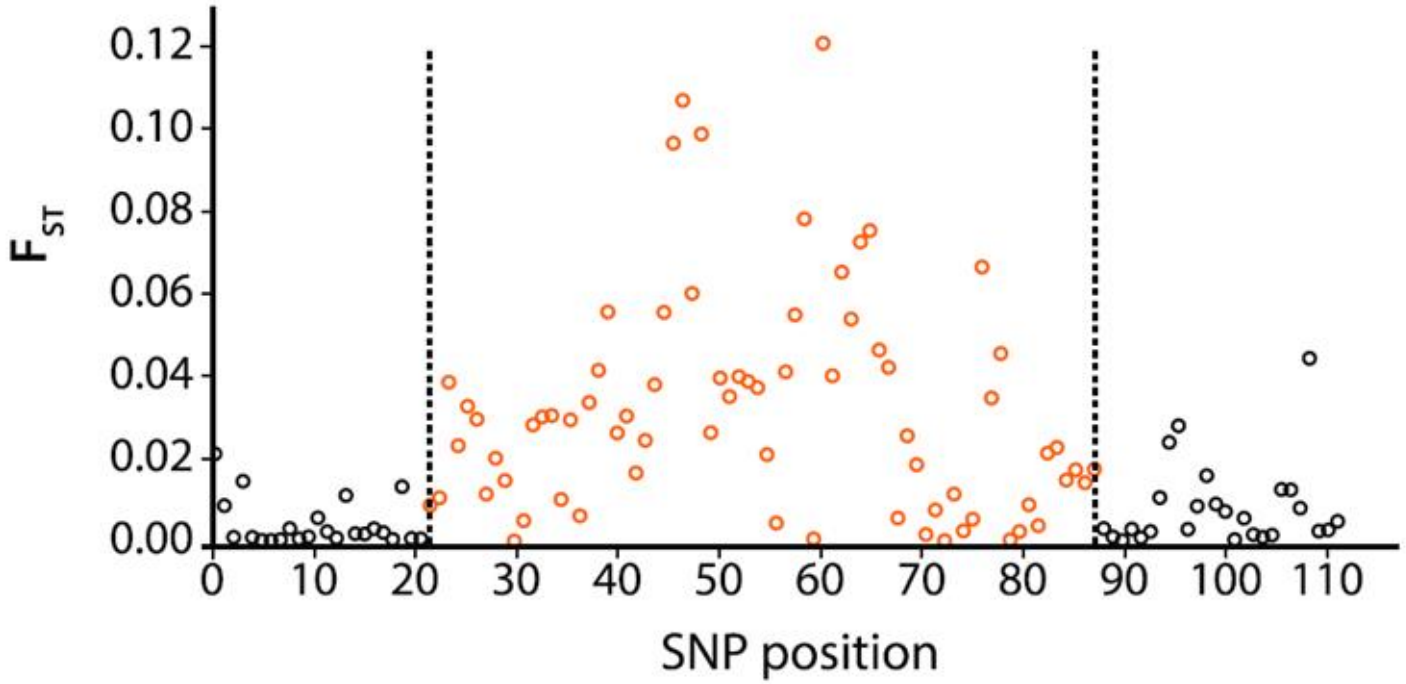
LOCUS F_{ST}


POP A
POP B
SNP 134
SNP 5466
SNP 6101
LOW
F_{ST}


POP A
POP B
SNP 8751
HIGH F_{ST}

F_{ST} OUTLIERs

Loci putatively under selection



Genomic basis of adaptation

Soria-Carrasco et al. Science 2014

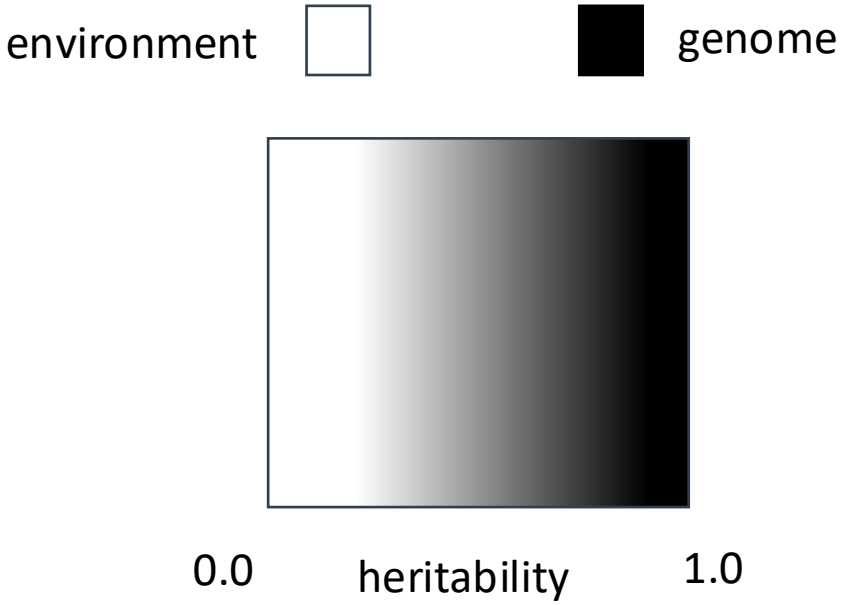
Heritability, genetic architecture and main genetic interactions

- heritability
- additive genetic variation
- epistasis
- pleiotropy
- “trade off”

The evolution of the phenotypic trait is influenced by (additive) genetic variation

Heritability is a concept that summarizes how much of the variation in a trait is due to variation in genetic factors.

Heritability is not the proportion of a phenotype that is genetic !



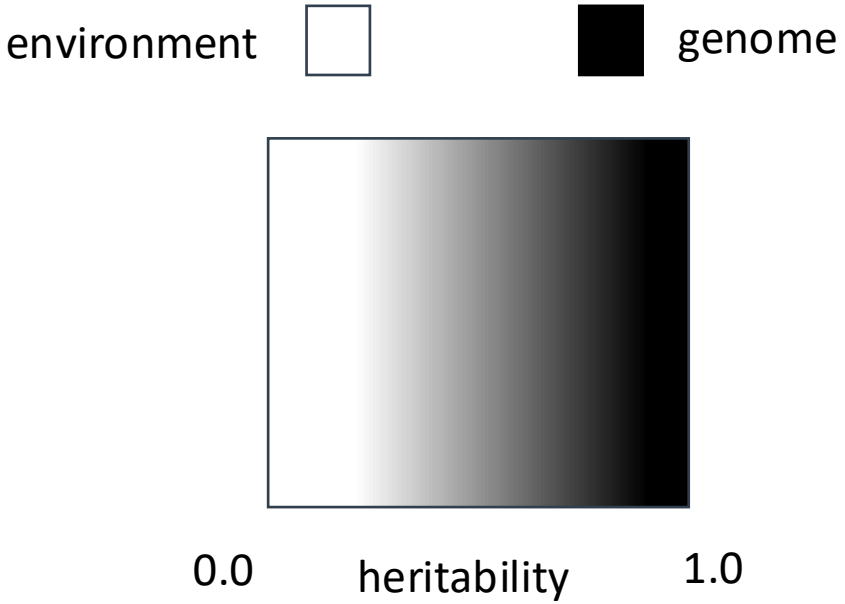
An estimate of the heritability of a trait is specific to one population in one environment, and it can change over time as circumstances change. Heritability estimates range from zero to one. Being close to zero indicates that almost all of the **variability in a trait** among individuals is due to environmental factors, with very little influence from genetic differences.

Heritability is about what determines **the variance of the distribution** and not the mean!

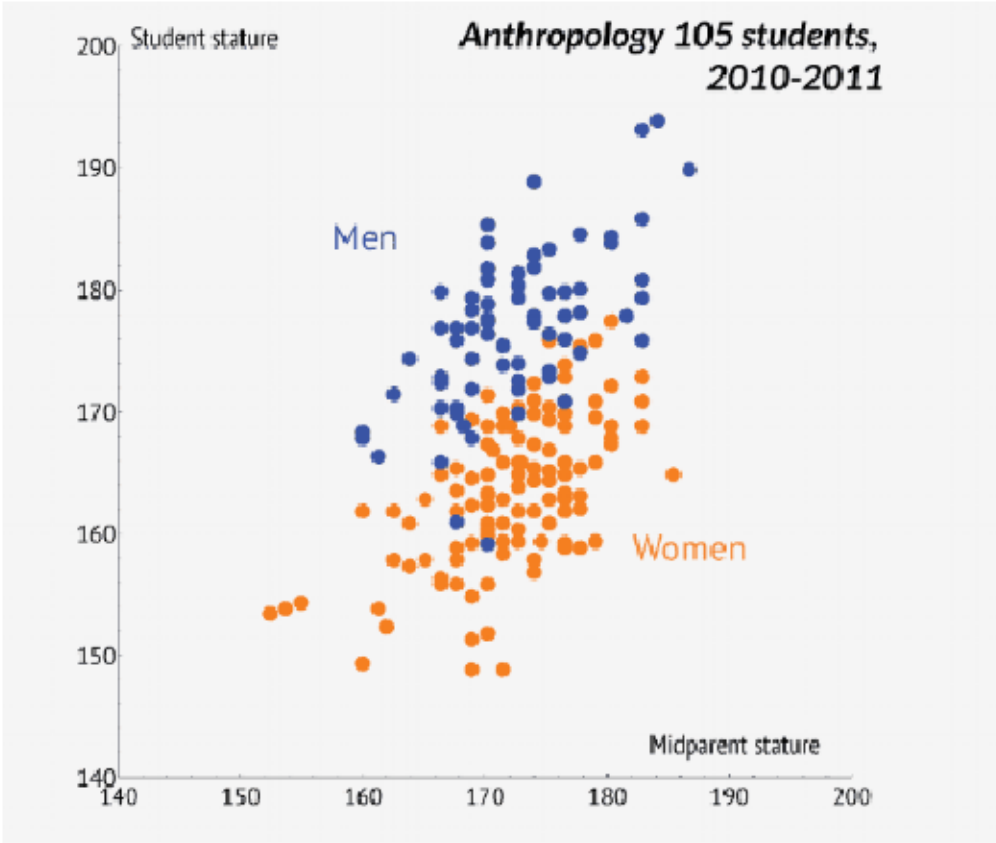
NATURE OR NURTURE

Heritability is a concept that summarizes how much of the variation in a trait is due to variation in genetic factors.

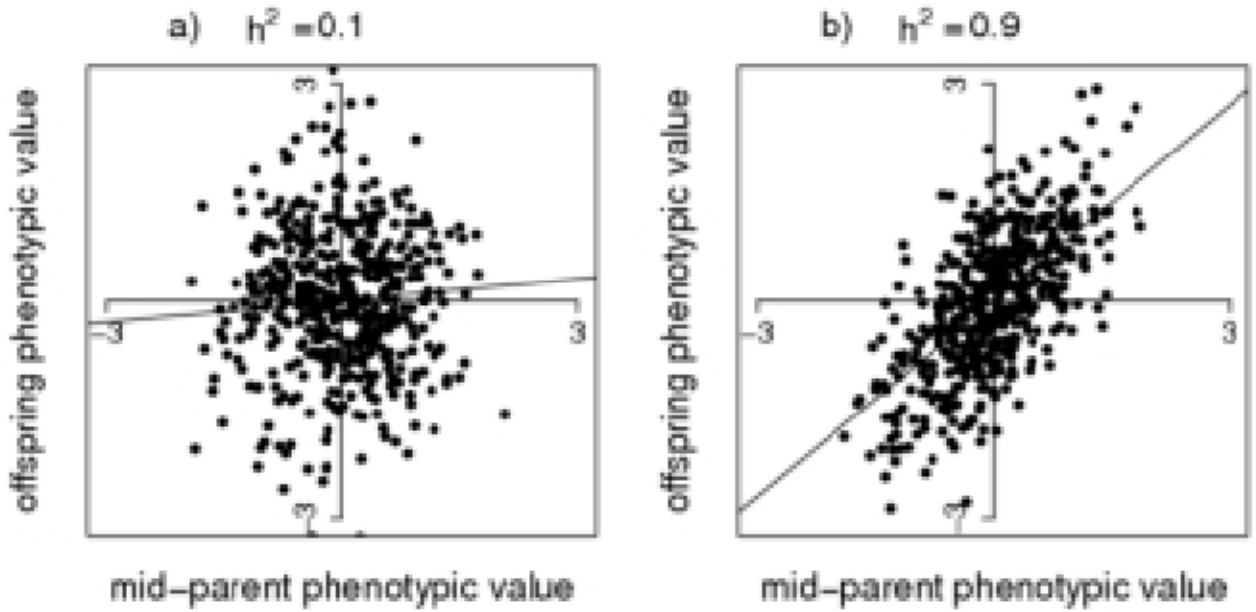
Heritability is not the proportion of a phenotype that is genetic !



Traits under strong directional selection can have low variability in population (harmful mutations purged out). Their mean value is under the strong genetic influence, but their heritability is often low, as their variance is mostly due to the environment (squirrel example later in the lecture)
E.g. traits strongly related to fitness- reproductive output, number of limbs…

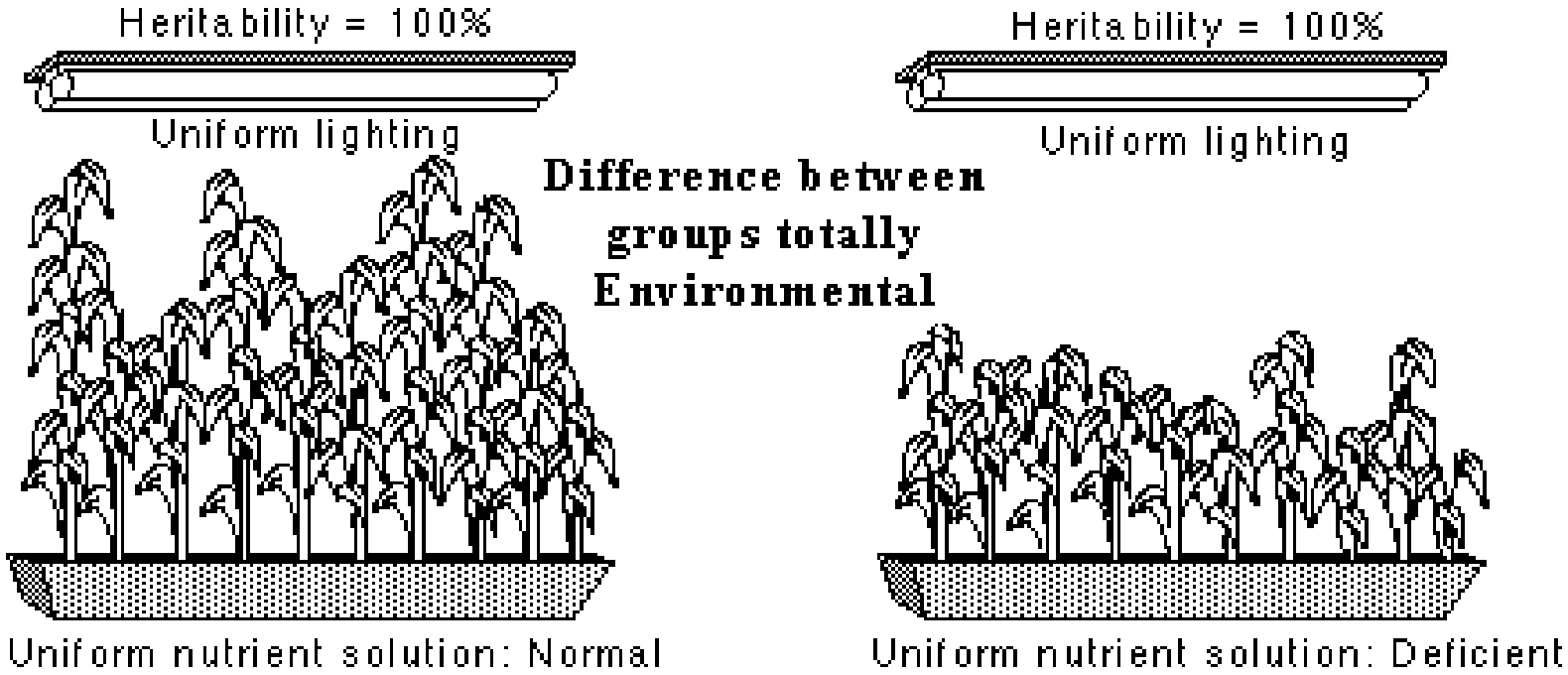


Heritability is often calculated as regression between mid value of parents and offspring



1969 Arthur Jensen “How much can we boost IQ and scholastic achievement? – rasism

1970 Lewontin – REBUTAL



The genetic variance can be divided into **additive genetic variance and non-additive genetic variance**

ADDITIVE GENETIC VARIANCE - alleles whose contributions to the trait are independent of other genes or the environment

aa ab bb

NON-ADDITIVE GENETIC VARIANCE all nonlinear genetic effects

- **dominance** (when presence of one allele has the same effect as two alleles)

  AA Aa aa

- **epistasis** (interactive effects of different genes, the phenotypic results of one gene iare influenced by other genes)
- **gene-environment effects** where the contribution of an allele changes depending on the environment.

The fraction of the variance explained by the additive genetic effects is called the **narrow-sense heritability** as opposed to the **broad-sense heritability**, which includes all the genetic effects.

The evolution of the phenotypic trait is influenced by (additive) genetic variation

- In the case of additive effects, alleles average effects are generally predictable across generations. This makes additive genetic variance the primary predictor of the response to selection

- In the case of dominance and epistasis (on-additive effects) offspring inherit alleles,but their contribution to the response to selection is generally more dependent on the genetic background, mating system, allele frequencies and recombination.

ROYAL SOCIETY OPEN SCIENCE

rsos.royalsocietypublishing.org

Parenting behaviour is highly heritable in male stickleback

Alison M. Bell[1,2,3,4,5], Rebecca Trapp[1] and Jason Keagy[1,2,3,4,5]

Research

Cite this article: Bell AM, Trapp R, Keagy J.

https://youtu.be/f0natXGHyNw

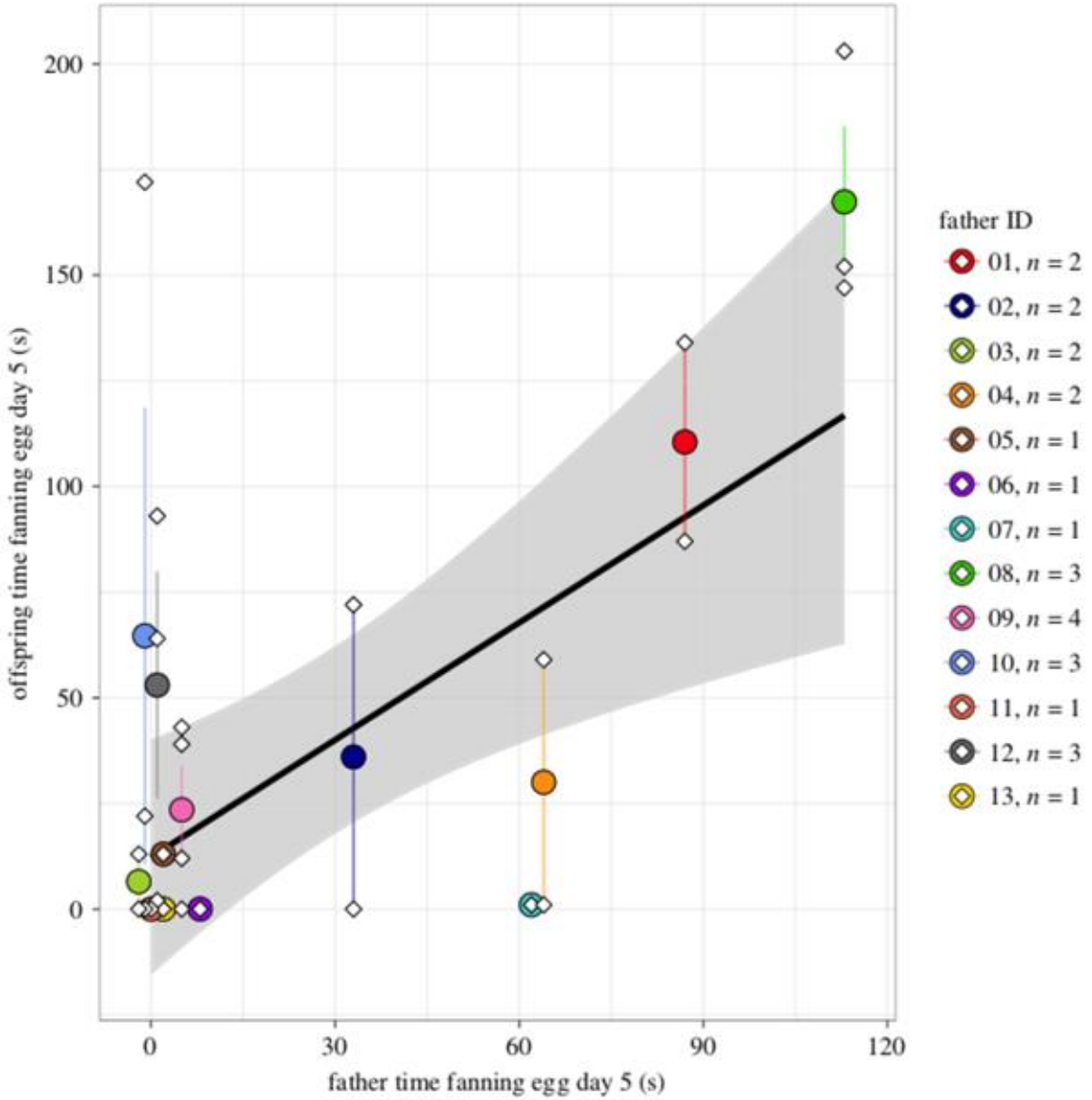


Figure 2. Relationship between fanning in fathers and sons. Son fanning time plotted against father fanning time. For visualization, the regression line is in black and 95% CI are indicated in grey (linear regression: $\beta = 0.92 \pm 0.27, t_{11} = 3.48, p = 0.005$). Solid circles and lines indicate means ± s.e. for each family. Individual data points are indicated with diamonds. Legend shows the number of offspring per family, and colour coded as in figure 1.

- Heritabilities close to 1 suggest a very simple genetic basis
- theory predicts that because natural selection removes genetic variation, traits under weak selection are expected to be more heritable than traits under strong selection
- **weaker selection because its exerted only in males**
- parenting behaviour is also a example of indirect genetic effects (**IGEs**)— when traits in one individual are influenced by genes in another individual
- a highly heritable component to parenting behaviour could have implications for sexual selection.

time spent in parental behaviour in fathers and sons (*fanning*)

Ecol Evol. 2014 May; 4(10): 1729–1738.
Published online 2014 Apr 11. doi: [10.1002/ece3.982]
PMCID: PMC4063471
PMID: 24963372

Very low levels of direct additive genetic variance in fitness and fitness components in a red squirrel population



Evolutionary potential of any trait in population depends on its genetic diversity- main material for selection

A trait must genetically correlate with fitness in order to evolve in response to natural selection, but theory suggests that strong directional selection should erode additive genetic variance in fitness and limit future evolutionary potential.

- Fitness is a measure of the extent to which individuals contribute genes to the next generation through the processes of survival and reproduction
- The resemblance between parents and offspring is entirely due to the additive effect that genes have on phenotype.

Estimates of heritability (h^2), maternal effects (m^2), and of variance components, including additive genetic (V_a), maternal (V_m), residual (V_r), and credible intervals (CI) are reported for lifetime reproductive success (LRS) of North American red squirrels (*Tamiasciurus hudsonicus*). Additionally, we report the mean, standard deviation, median, and number of individuals measured for each fitness component

Fitness component	Mean ± SD	Median	*N*	h^2	CI	m^2	CI
LRS	1.1 ± 3.5	0	2981	4.90E−04	3.0E−08 to 0.07	0.07	0.02 to 0.14
Female LRS	1.4 ± 3.9	0	2133	6.80E−04	8.5E−11 to 0.10	0.08	0.01 to 0.14
Male LRS	0.3 ± 1.6	0	848	1.10E−03	7.1E−10 to 0.39	0.10	0.10 to 0.37
Mast LRS	1.5 ± 3.9	0	756	1.20E−03	1.8E−10 to 0.29	0.11	0.01 to 0.23
Nonmast LRS	1.0 ± 3.3	0	2225	1.60E−04	4.5E−13 to 0.06	0.12	0.04 to 0.21

LRS (lifetime reproductive success) – higher in mast years- food resources are superabundant.

Heritability of 0.00049 for LRS.

275 generations for the average lifetime reproductive success to increase by one pup.

LETTER

doi:10.1038/nature12489

Life history trade-offs at a single locus maintain sexually selected genetic variation

Susan E. Johnston[1,2]†, Jacob Gratten[1,3]†, Camillo Berenos[2], Jill G. Pilkington[2], Tim H. Clutton-Brock[4], Josephine M. Pemberton[2] & Jon Slate[1]

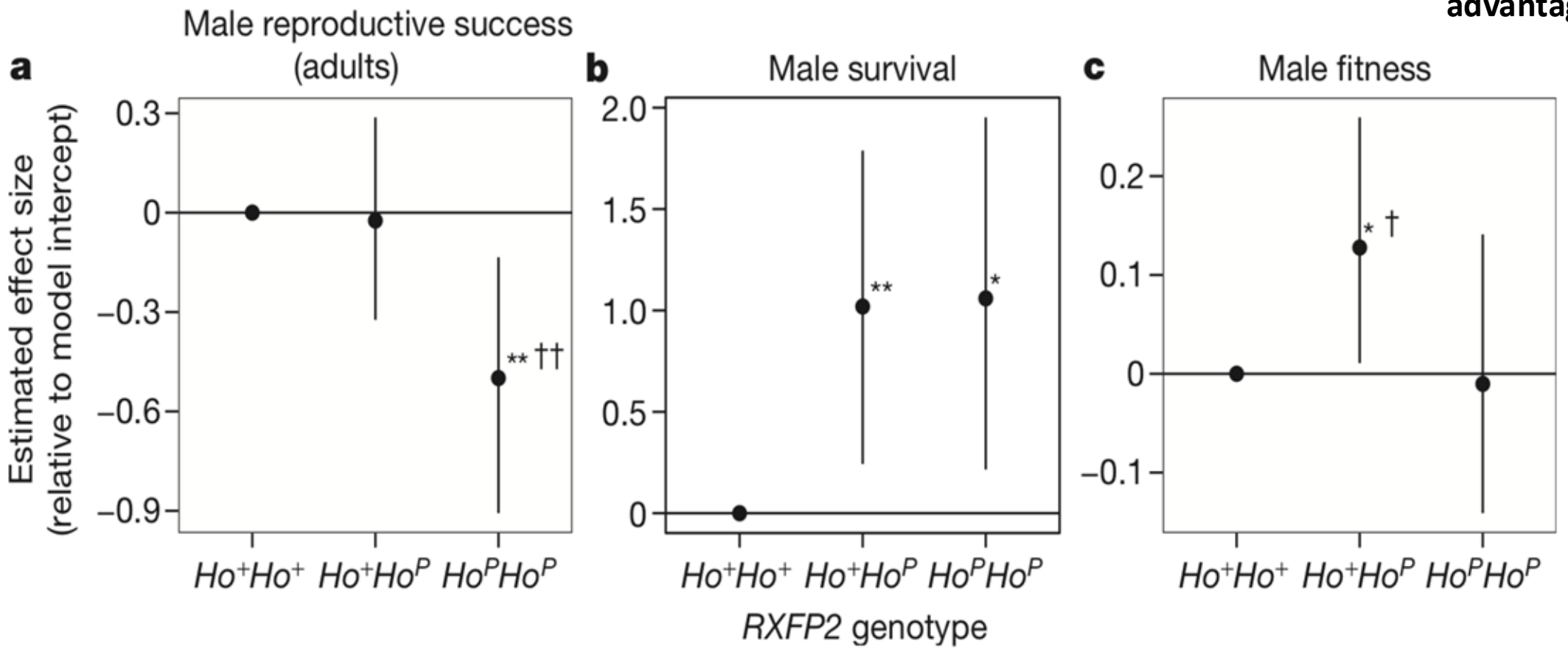


Figure 1 | Horn morphology variation with *RXFP2* genotype. Examples of adult male horn morphology with their corresponding *RXFP2* genotypes. **a**, Four-year-old normal-horned $Ho^{+}Ho^{+}$. **b**, Five-year-old normal-horned $Ho^{+}Ho^{P}$. **c**, Five-year-old normal-horned $Ho^{P}Ho^{P}$. **d**, Three-year-old scurred $Ho^{P}Ho^{P}$.

„Trade-off"
large horns increase reproductive success, small horns increase survival – heterozygotes have highest fitness

In wild Soay sheep, ***large horns confer an advantage in strong intra-sexual competition****, yet males show an inherited polymorphism for horn type and have substantial genetic variation in their horn size[6]. Here we show that most genetic variation in this trait is maintained by a* ***trade-off between natural and sexual selection at a single gene****, relaxin-like receptor 2 (RXFP2). We found that an allele conferring larger horns,* ***Ho_1****, is associated with* ***higher reproductive success****, whereas a smaller horn allele,* ***Ho_P****,* ***confers increased survival****, resulting in a net effect of overdominance (that is,* ***heterozygote advantage****) for fitness at RXFP2.*

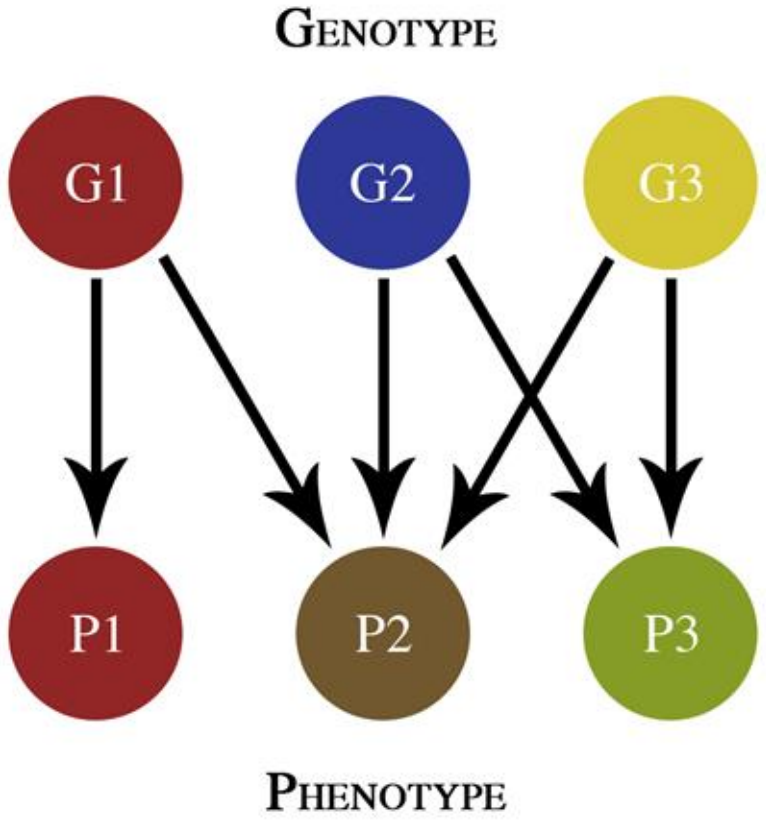
heterozygote advantage!



- sexually selected traits often exceed the point at which they would be optimal for survival, indicating that trade-offs exist between sexual and non-sexual fitness.
- same alleles found in mouse and human- related to bone density and sexual development

Pleiotropy is the property of genes affecting multiple functions or characters of an organism.

Trade off - when contributing more to one function detracts from allocation to the second function – **antagonistic pleiotropy.**



Genetic loci associated with coronary artery disease harbor evidence of selection and antagonistic pleiotropy

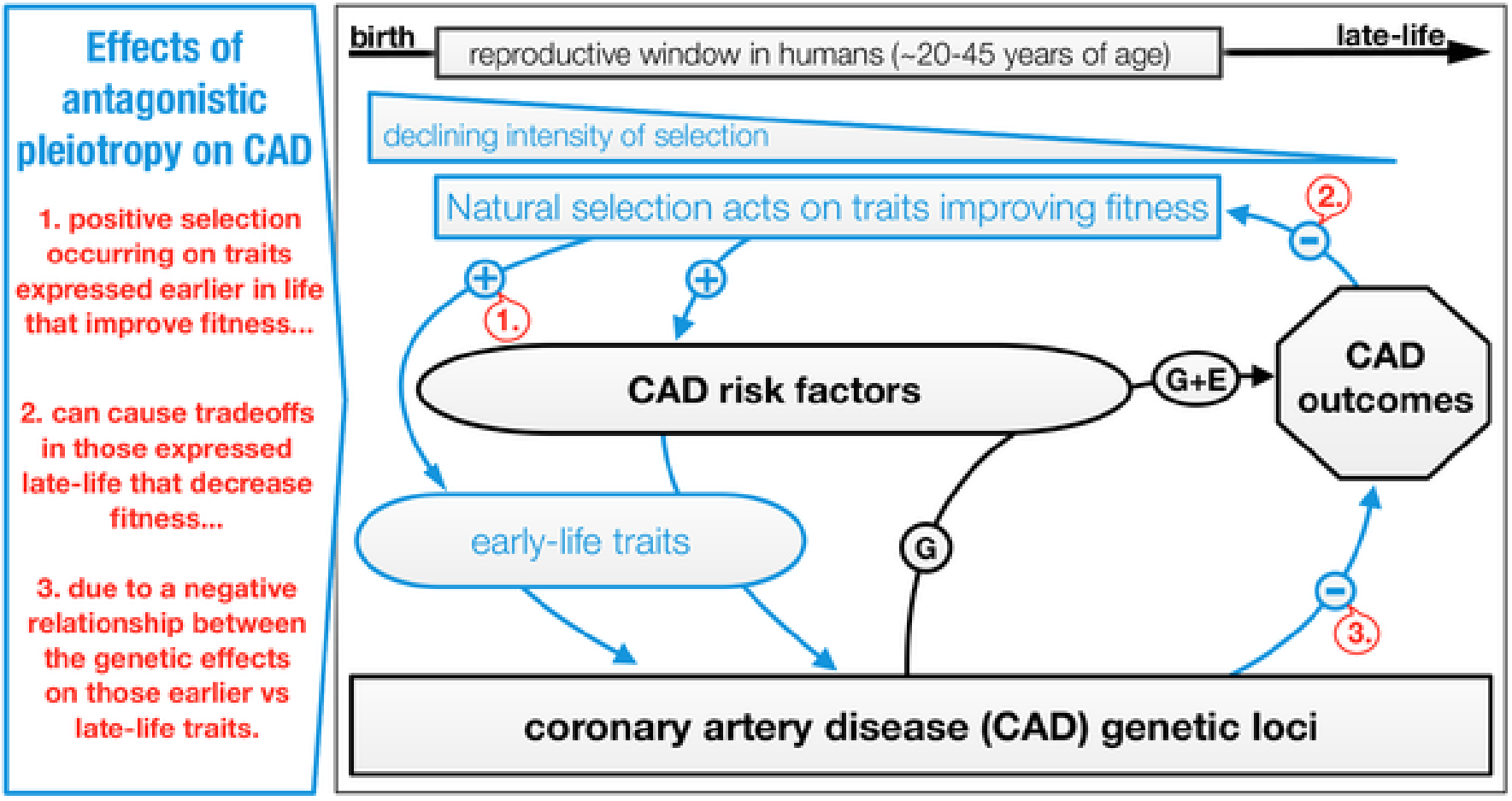
Sean G. Byars, Qin Qin Huang, Lesley-Ann Gray, Andrew Bakshi, Samuli Ripatti, Gad Abraham, Stephen C. Stearns, Michael Inouye

Published: June 22, 2017 • https://doi.org/10.1371/journal.pgen.1006328 • >> See the preprint

natural selection maintains alleles responsible for cardiovascular diseases as they have positive effect on human reproduction

„One of the fundamental questions about CAD—whose progression begins in young adults with arterial plaque accumulation leading to life-threatening outcomes later in life—**is why natural selection has not removed or reduced this costly disease**. It is the leading cause of death worldwide and has been present in human populations for thousands of years, implying considerable pressures that natural selection should have operated on. Our study provides new evidence that genes underlying CAD have recently been modified by natural selection and that these **same genes uniquely and extensively contribute to human reproduction,** which suggests that natural selection may have maintained genetic variation contributing to CAD because of its beneficial effects on fitness. This study provides novel evidence that **CAD has been maintained in modern humans as a by-product of the fitness advantages those genes provide early in human lifecycles**."

Fig 5. Conceptual figure of potential evolutionary tradeoffs between coronary artery disease (CAD) burden and other phenotypes as a consequence of antagonistic pleiotropy (AP) [42].



negative relationship betwee genetic effects on early vs late-life traits

Byars SG, Huang QQ, Gray LA, Bakshi A, Ripatti S, et al. (2017) Genetic loci associated with coronary artery disease harbor evidence of selection and antagonistic pleiotropy. PLOS Genetics 13(6): e1006328. https://doi.org/10.1371/journal.pgen.1006328
https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1006328

PLOS | GENETICS

Review

Pleiotropy in the melanocortin system, coloration and behavioural syndromes

Anne-Lyse Ducrest, Laurent Keller and Alexandre Roulin

Covariation between coloration and behavioural, physiological and morphological traits is affected by eumelanin production

Table 2. Summary of the covariation between eumelanin-based coloration and behavioural, physiological and morphological traits in wild vertebrates reported in Supplementary Table S2

Category of traits	Phenotypes	Sign of covariation	N[a]
Sexual traits	Sexual behaviour	+	9
		–	0
	Plasma testosterone level	+	4
		–	0
Aggressiveness and exocrine gland activity	Aggressiveness	+	18
		–	2
	Mass of uropygial gland	+	0
		–	1
Stress response	Resistance to stressors	+	6
		–	0
Immune system	Immune response against nonpathogenic antigen	+	1
		–	0
Energy homeostasis	Metabolic rate	+	2
		–	0
	Body mass	+	7
		–	3
	Body size	+	7
		–	1

[a]Number of studies showing a significant positive or negative correlation between eumelanin-based coloration and other phenotypic attributes.

Review

Cell PRESS

Pleiotropy in the melanocortin system, coloration and behavioural syndromes

Anne-Lyse Ducrest, Laurent Keller and Alexandre Roulin

„A review of the literature indeed reveals that, as predicted, ***darker wild vertebrates are more aggressive, sexually active and resistant to stress*** *than lighter individuals.* ***Pleiotropic effects of the melanocortins*** *might thus account for the widespread covari- ance between melanin-based coloration and other phenotypic traits in vertebrates. „*

POMC gene is responsible for melanocortin production, which attaches to 5 different receptors in many tissues. Antagonistic proteins are ASIP i AGRP proteins, and they also modulate its effect in specific tissues (epistasis).

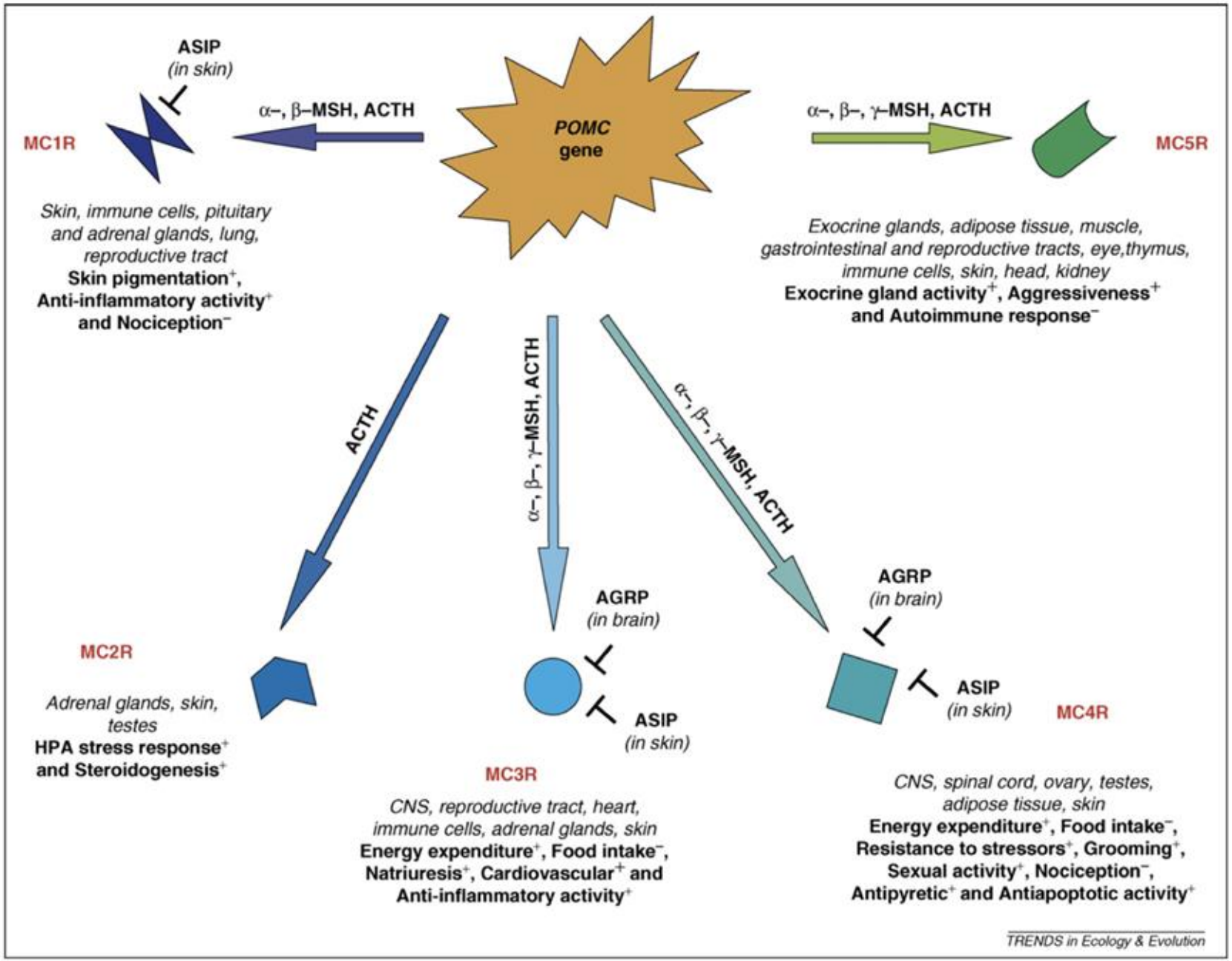


Figure 3. Melanocortin system. The *proopiomelanocortin* (*POMC*) gene produces the melanocortins (α-, β- and γ-MSH and ACTH) which bind to five melanocortin receptors (MC1–5R). Location of these five receptors in vertebrates is given in italics while their function is written in bold. For each function, we report whether binding of the melanocortins to the different MCRs has positive (+) or negative effects (–). For example, binding of melanocortins to MC4R increases energy expenditure but reduces food intake. The agonists and inverse antagonists (agouti-signalling protein, ASIP or agouti-related protein, AGRP) for each MCRs are indicated with the symbol ⊥.

REPORT | WILDLIFE DISEASE

Disease outbreaks select for mate choice and coat color in wolves

SARAH CUBAYNES, ELLEN E. BRANDELL, DANIEL R. STAHLER, DOUGLAS W. SMITH, EMILY S. ALMBERG, SUSANNE SCHINDLER, ROBERT K. WAYNE, ANDREW P. DOBSON, BRIDGETT M. VONHOLDT, [...], AND TIM COULSON +3 authors Authors Info & Affiliations



In North America, wolves generally have either gray or black coats, and the proportions of these colors vary across populations. The genetics of these coat colors have been revealed, and we now know that ***black wolves are either homozygous or heterozygous for a gene that is also related to resistance to canine distemper virus.*** *Analyzing data from across North America, but especially from populations in Yellowstone National Park, Cubaynes et al. found that black coats were maintained through* ***heterozygote advantage in, and mate choice preference for, black-coated wolves in areas where canine distemper is endemic even though gray-coated wolves have higher success when the virus is absent.*** *—SNV*

https://www.science.org/content/article/some-wolves-black-coat-isn-t-just-fashionable-it-s-lifesaver?fbclid=IwAR3yfolKkZKmheZSBL7cQDLLv6mv0D1hic_Ch-rqpahKNUrXs16AlhB_Y2k

Article | Published: 19 October 2022

Evolution of immune genes is associated with the Black Death

Jennifer Klunk, Tauras P. Vilgalys, Christian E. Demeure, Xiaoheng Cheng, Mari Shiratori, Julien Madej, Rémi Beau, Derek Elli, Maria I. Patino, Rebecca Redfern, Sharon N. DeWitte, Julia A. Gamble, Jesper L. Boldsen, Ann Carmichael, Nükhet Varlik, Katherine Eaton, Jean-Christophe Grenier, G. Brian Golding, Alison Devault, Jean-Marie Rouillard, Vania Yotova, Renata Sindeaux, Chun Jimmie Ye, Matin Bikaran, ... Luis B. Barreiro + Show authors

Nature **611**, 312–319 (2022) | Cite this article

122k Accesses | **3** Citations | **3781** Altmetric | Metrics



Infectious diseases are among the strongest selective pressures driving human evolution[1,2]. This includes the single greatest mortality event in recorded history, the first outbreak of the second pandemic of plague, commonly called the Black Death, which was caused by the bacterium Yersinia pestis[3]. This pandemic devastated Afro-Eurasia, killing up to 30–50% of the population[4]. To identify loci that may have been under selection during the Black Death, we characterized ***genetic variation around immune-related genes from 206 ancient DNA extracts, stemming from two different European populations before, during and after the Black Death****. Immune loci are strongly enriched for highly differentiated sites relative to a set of non-immune loci,* ***suggesting positive selection****. We identify 245 variants that are highly differentiated within the London dataset, four of which were replicated in an independent cohort from Denmark, and represent the strongest candidates for positive selection. The selected allele for one of these variants,* ***rs2549794****, is associated with the production of a full-length (versus truncated) ERAP2transcript,* ***variation in cytokine response to Y. pestis*** *and increased ability to control intracellular Y. pestis in macrophages. Finally, we show* ***that protective variants overlap with alleles that are today associated with increased susceptibility to autoimmune diseases, providing empirical evidence for the role played by past pandemics in shaping present-day susceptibility to disease***



Evolution of Human-Specific Alleles Protecting Cognitive Function of Grandmothers

*According to the paper, a **mutant form of an immune receptor**, found in roughly **one fifth of people**, helps the immune system detect Neisseria gonorrhoeae, the bacteria responsible for the sexually transmitted disease. Typically, white blood cells particularly monocytes and macrophages, use a receptor called CD33, to distinguish between host cells and unwelcome pathogens invading the body. When CD33 binds to sialic acids—sugars that tend to adorn the membranes of host cells, acting as a molecular ID— immune cells recognize those cells and prevent the immune system from launching an attack.*

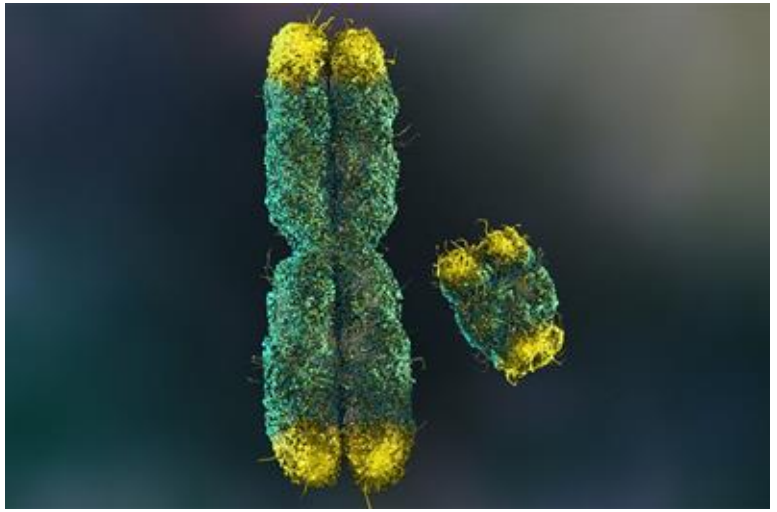
In the brain, immune cells called microglia help remove damaged material and amyloid plaques. Normal CD33 signalling can inhibit some of this activity. The variant can reduce that inhibitory effect, potentially allowing microglia to clear harmful material more effectively.

https://doi.org/10.1093/molbev/msac151

NEWS | BIOLOGY

Men lose Y chromosomes as they age. It may be harming their hearts

Study in mice is first to directly test health effects of losing male chromosome



DOI: 10.1126/science.abn3100

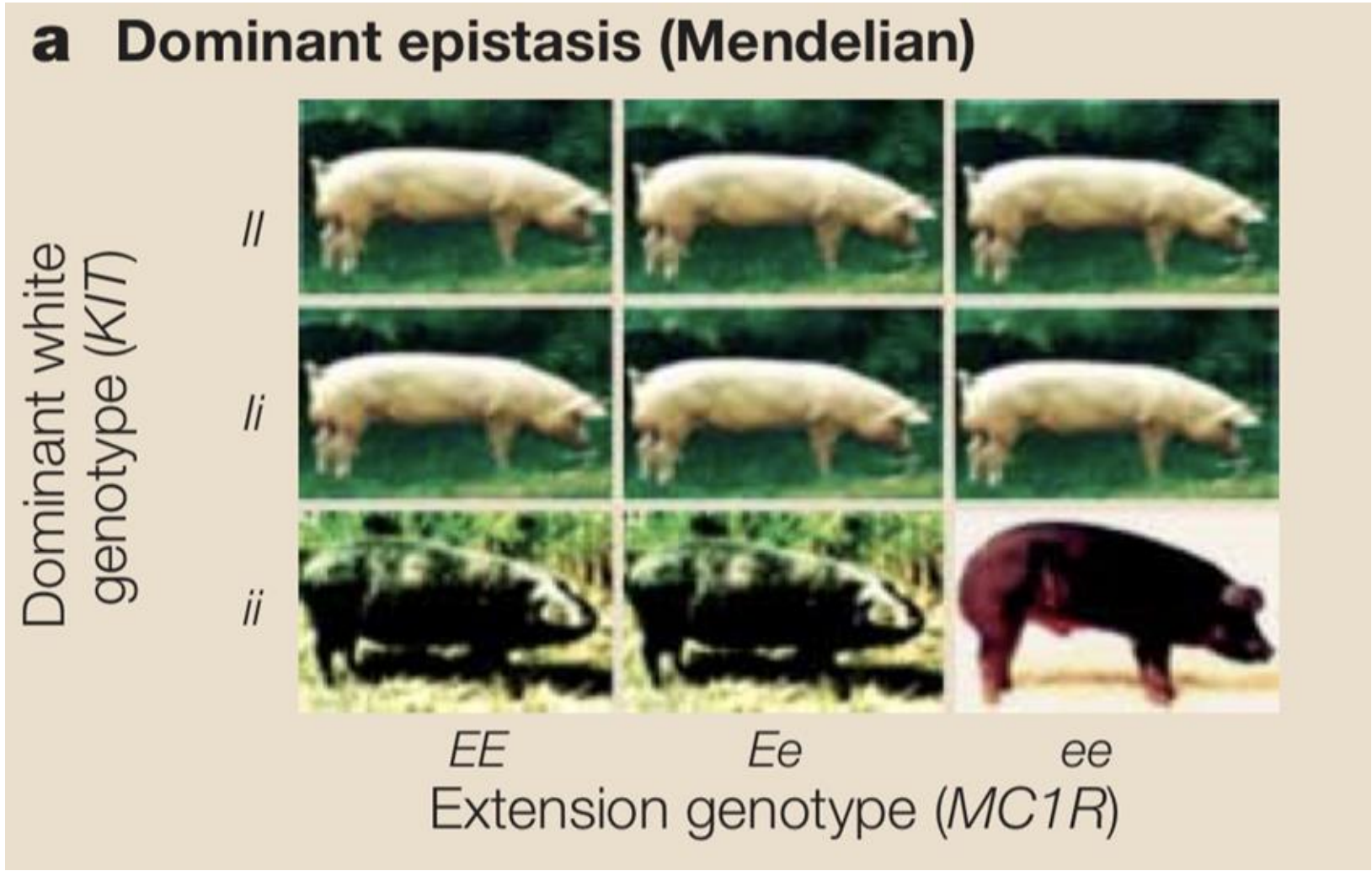
To test whether removing the Y chromosome harms health, Walsh and colleagues performed bone marrow transplants on 38 mice. They used the CRISPR-Cas9 gene-editing tool to ***delete the Y chromosome*** *from mouse bone marrow cells and then inserted the altered cells into young male mice whose bone marrow had been removed. The swap didn't banish the Y chromosome from the recipients, but it* ***culled the chromosome from 49% to 81% of white blood cells****—about the same percentage as in many humans with Y-chromosome loss. The 37 control mice for this experiment also received bone marrow transplants but retained the Y chromosome.* ***Mice that lost their Y chromosome also had weaker hearts.*** *After about 15 months, the heart's contraction strength had declined by close to 20%. In addition, the buildup of tough connective tissue, a process called fibrosis, surged in the hearts of mice missing the Y chromosome. This accumulation stiffens the heart and impairs its ability to pump blood.*

Walsh and colleagues obtained DNA and survival information for more than 15,000 men from the UK Biobank, a huge health database. The team determined that men who had lost the Y chromosome from at least 40% of their white blood cells were 31% more likely to die from circulatory system diseases than those in which the chromosome was more abundant.

Epistasis

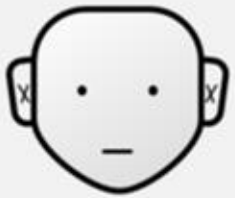
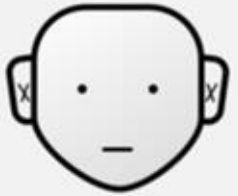
- fitness of one allele is affected by alleles on other loci

- ‘stressful’ context (genetic or environmental) is one in which the absolute fitness of the wild-type is reduced relative to its absolute fitness in some other reference context. Changes in the environment such as a reduction in food abundance, an increase in natural enemies, or exposure to extreme temperatures or toxic chemicals
- in the context of adaptation to multiple stresses, fitness can also be impacted by epistatic interactions between mutations, where a fitness effect of one mutation is moderated by the presence of mutations at other loci



the dominant allele (*I*) at the *KIT* locus, which confers white-coat colour in the pig, is dominant over all alleles at the *MC1R* locus (*E*), which confer a darker coat colour.

genes for baldness are dominant over the genes for hair color

	Gene for blond hair	Gene for red hair
	 Blond hair	 Red hair
+ Gene for baldness	 Bald	 Bald

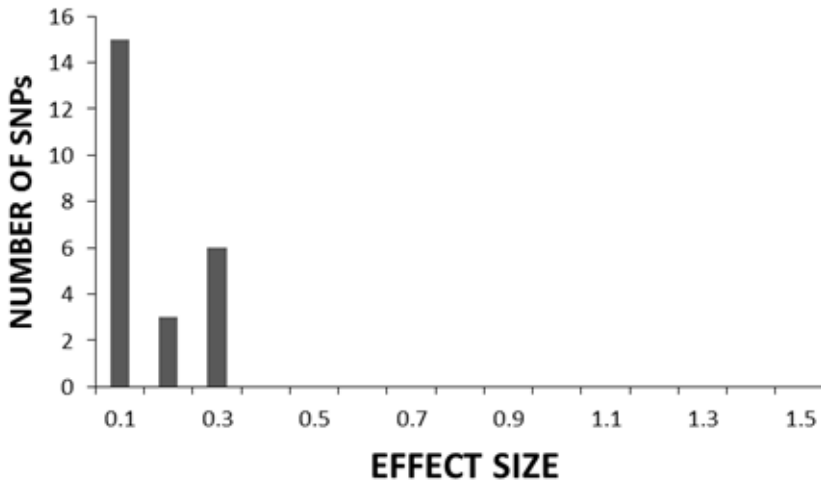
Genetic architecture of phenotypic traits

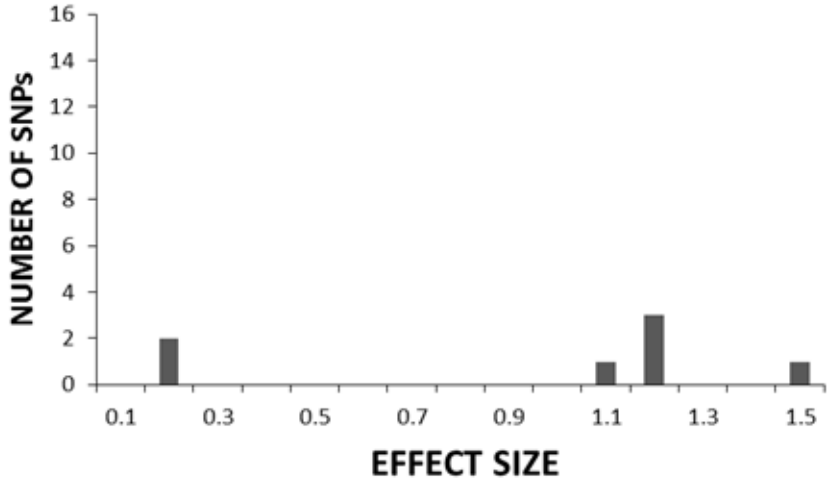
Genetic architecture describes the characteristics of genetic variation that are responsible for heritable phenotypic variability.

It depends on the **number of genetic variants affecting a trait**, their frequencies in the population, the **magnitude of their effects** and their interactions with each other and the environment.

Genetic architecture is often described as **monogenic, oligogenic or polygenic**, meaning that one, few or many genetic variants contribute to phenotypic variability, respectively.

Genetic architecture of phenotypic traits





POLIGENIC – many loci of small effect

OLIGOGENIC – small number of genes of higher effect

The strengths of the effect (x) and the number of genetic variants that determine the phenotypic trait(y)

Genetic architecture of phenotypic traits

GWAS - Genome Wide Association mapping

complex algorithms determine the alleles whose frequencies coincide/correlate with phenotypic traits

Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior

Andrea Ganna[1,2,3,4,*], Karin J. H. Verweij[5,*], Michel G. Nivard[6], Robert Maier[1,2,3], Robbee Wedow[1,3,7,8,9,10,11], ...
+ See all authors and affiliations

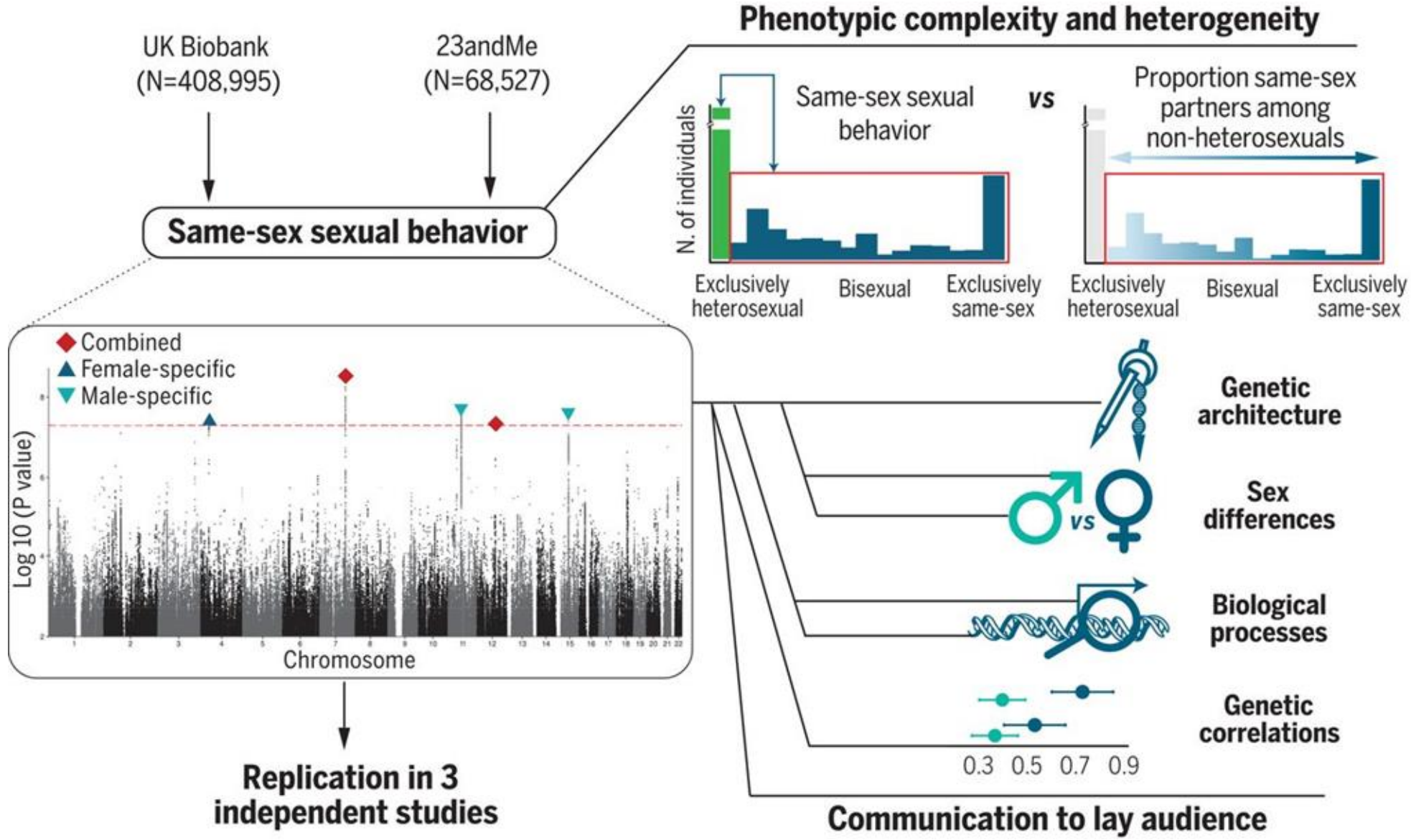
Science 30 Aug 2019:
Vol. 365, Issue 6456, eaat7693
DOI: 10.1126/science.aat7693

The genetics of sexual orientation

Twin studies and other analyses of inheritance of sexual orientation in humans has indicated that same-sex sexual behavior has a genetic component. Previous searches for the specific genes involved have been underpowered and thus unable to detect genetic signals. Ganna *et al.* perform a genome-wide association study on 493,001 participants from the United States, the United Kingdom, and Sweden to study genes associated with sexual orientation (see the Perspective by Mills). They find multiple loci implicated in same-sex sexual behavior indicating that, like other behavioral traits, nonheterosexual behavior is polygenic.

Science, this issue p. **eaat7693**; see also p. **869**

„The team analysed the genomes of 477,522 people who said they had had sex at least once with someone of the same sex, then compared these genomes with those of 358,426 people who said they'd only had heterosexual sex. "


UK Biobank
(N=408,995)
23andMe
(N=68,527)
Same-sex sexual behavior
Phenotypic complexity and heterogeneity
N. of individuals
Same-sex sexual behavior
vs
Proportion same-sex partners among non-heterosexuals
Exclusively heterosexual
Bisexual
Exclusively same-sex
Exclusively heterosexual
Bisexual
Exclusively same-sex
Combined
Female-specific
Male-specific
Log 10 (P value)
Chromosome
Genetic architecture
Sex differences
vs
Biological processes
Genetic correlations
0.3 0.5 0.7 0.9
Replication in 3 independent studies
Communication to lay audience

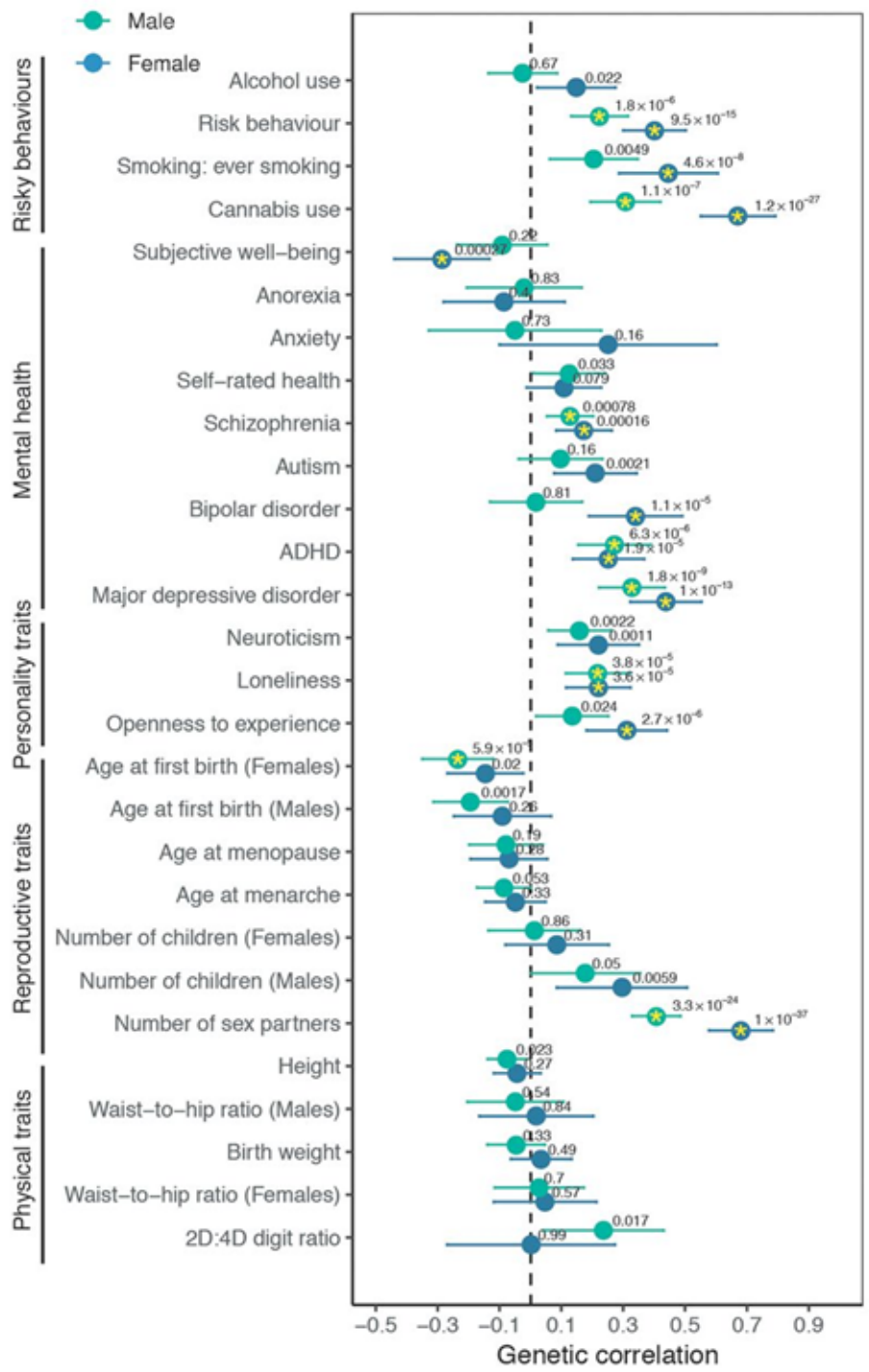


Fig. 4 Genetic correlations of same-sex sexual behavior with various preselected traits and disorders, separately for males and females.

Males, green; females, blue. Yellow asterisks denote the genetic correlations that were experiment-wise significant ($P < 8.9 \times 10^{-4}$; references, definitions, and full results can be found in table S19). Wald test *P* values for the genetic correlations are reported above each dot. Horizontal bars represent 95% CIs.

LIFE — JULY 26, 2022

Blocking a single gene awakens same-sex behavior in male fruit flies

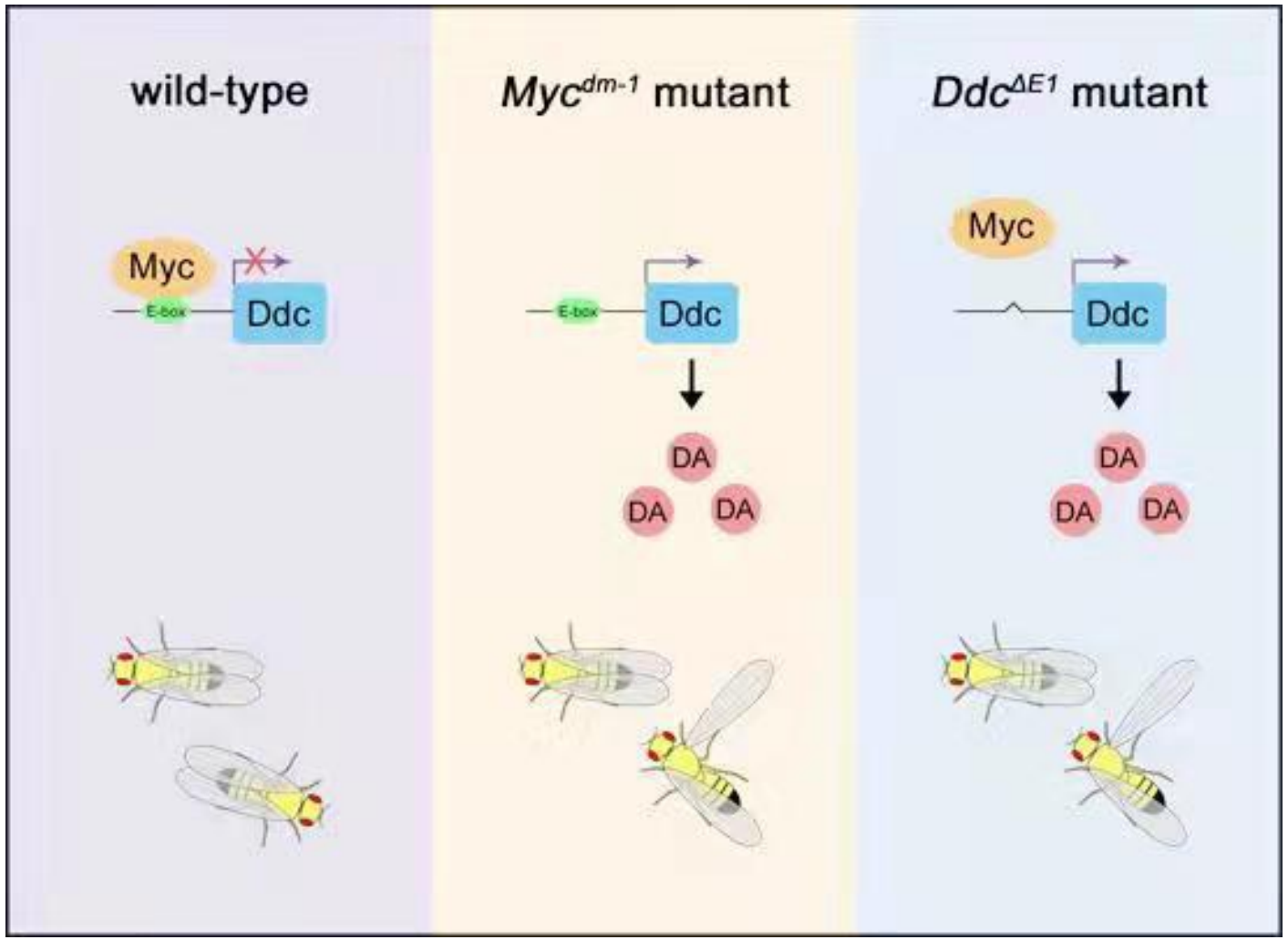
Turning off a gene called "Myc" has a surprising effect in male fruit flies: They start courting other males.



Credit: Studiotouch / Adobe Stock

While a team of Chinese researchers was studying the role of a gene called "Myc" in the development of cancer in fruit flies, they noticed an unusually high level of male-male sexual behavior. But this only occurred among males that carried mutations in the Myc gene.
Under normal circumstances, the protein produced by the Myc gene blocks the expression of another gene called Ddc. This blocks the formation of dopamine, a neuromodulatory molecule known to facilitate courtship behavior in different species, including fruit flies and humans. Dopamine also inhibits male-male courtship in fruit flies. But when Myc is missing, dopamine is produced, and males start courting each other.

https://doi.org/10.15252/embj.2021109905



Drosophila Myc is required in the nervous system to prevent male–male courtship in a DOPA decarboxylase (Ddc)-dependent manner, and drug-mediated Myc depletion in adult neurons suffices to elicit male–male courtship.

- Drosophila Myc is required in the nervous system to prevent male–male courtship.
- DOPA decarboxylase (Ddc) is necessary and sufficient for loss-of-Myc-induced male–male courtship.
- Myc directly inhibits Ddc transcription by binding to a Myc target site (E-box) in the Ddc promoter.
- Drug-mediated Myc depletion in adult neurons suffices to elicit male–male courtship.

Quantitative trait

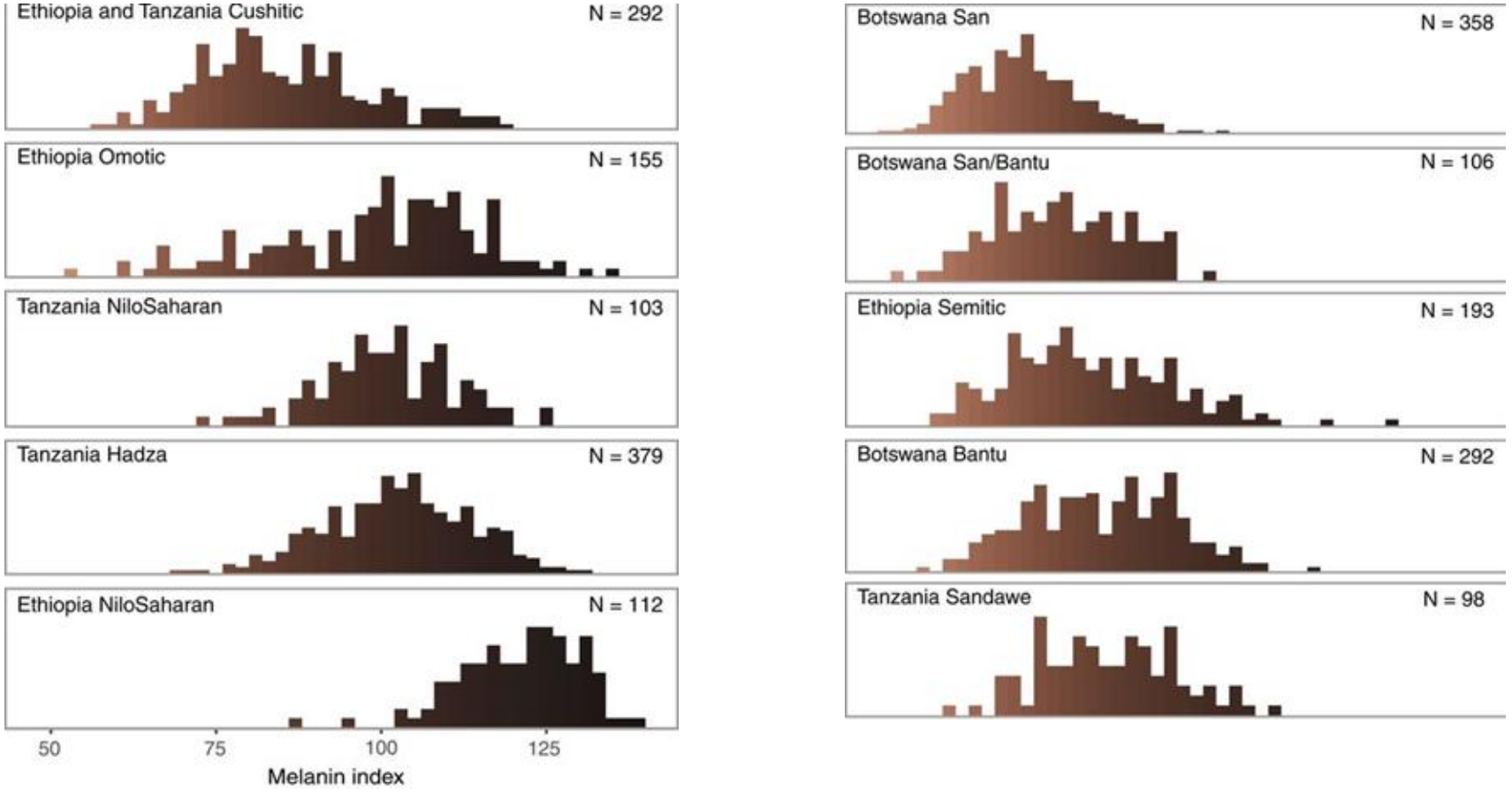
A quantitative trait is a measurable phenotype that **depends on the cumulative actions of many genes and the environment**. These traits can vary among individuals, over a range, to produce a continuous distribution of phenotypes. Examples include height, weight and blood pressure.

-**complex traits**, traits that do not behave according to simple Mendelian inheritance laws!



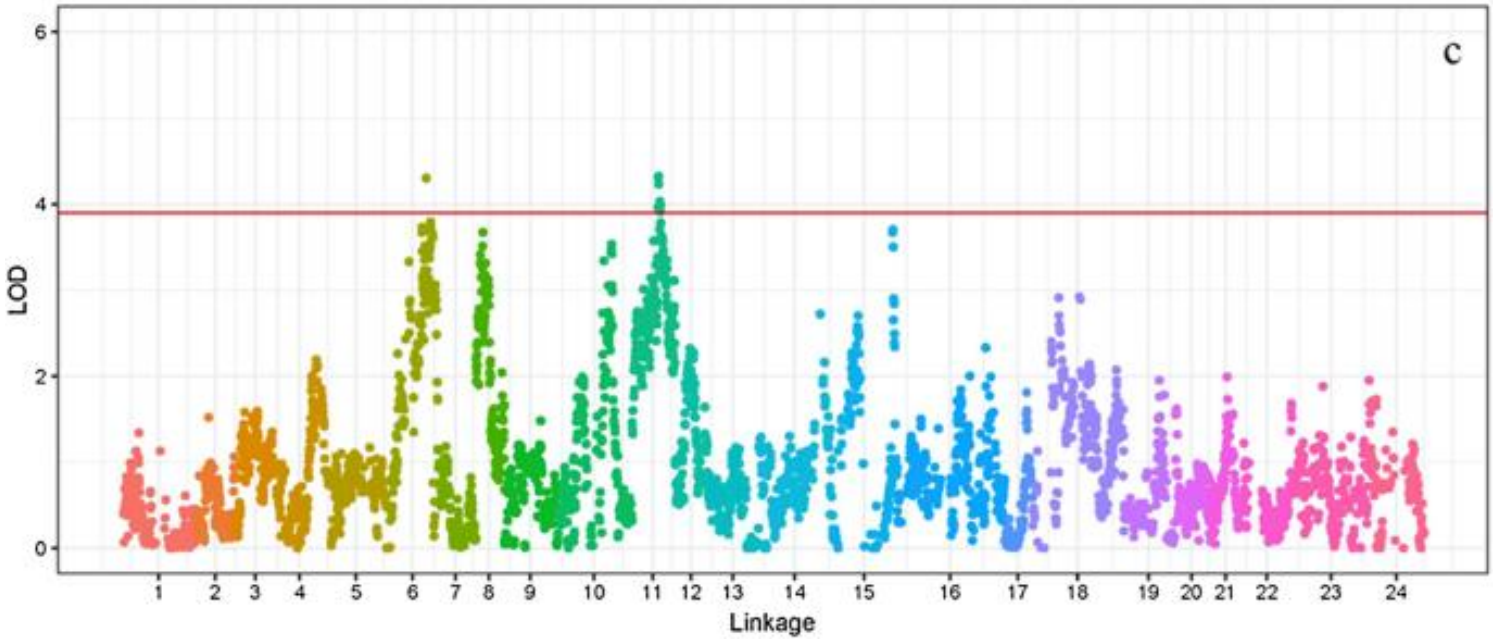


Quantitative traits – continuous distribution



Histogram of melanin index in 10 African human populations

Quantitative traits





the effect of specific loci across 24 chromosomes on the mass of *Larimichthys polyactis* individuals

QTL – *quantitative trait locus* – part of the chromosome that has an effect on the variation in the quantitative trait

Monogenic traits

Roaming Romeos: male crickets evolving in silence show increased locomotor behaviours

Susan L. Balenger*, Marlene Zuk

Department of Ecology, Evolution and Behavior, University of Minnesota, Twin Cities, MN, U.S.A.



- A mutation has changed the structure of the male crickets' wings, so that they are now born without the ability to chirp.
- cricket mating happens at night in the dark
- their song attracts a less welcome female: parasitic flies, whose larvae devour and kill the crickets from the inside out

- „It appears that they hang around singing males and intercept females that come in…In effect, they parasitise the songs of the singing males. It's a bit sneaky."
- **single mutation to produce flat wings**- but different mutations on two islands – **CONVERGENT EVOLUTION**
- directional selection on Kauai for males to respond to a silent environment by increasing their mobility, thus compensating for their lack of song and increasing their chance of encountering receptive females.
- https://www.nature.com/news/evolution-sparks-silence-of-the-crickets-1.15323