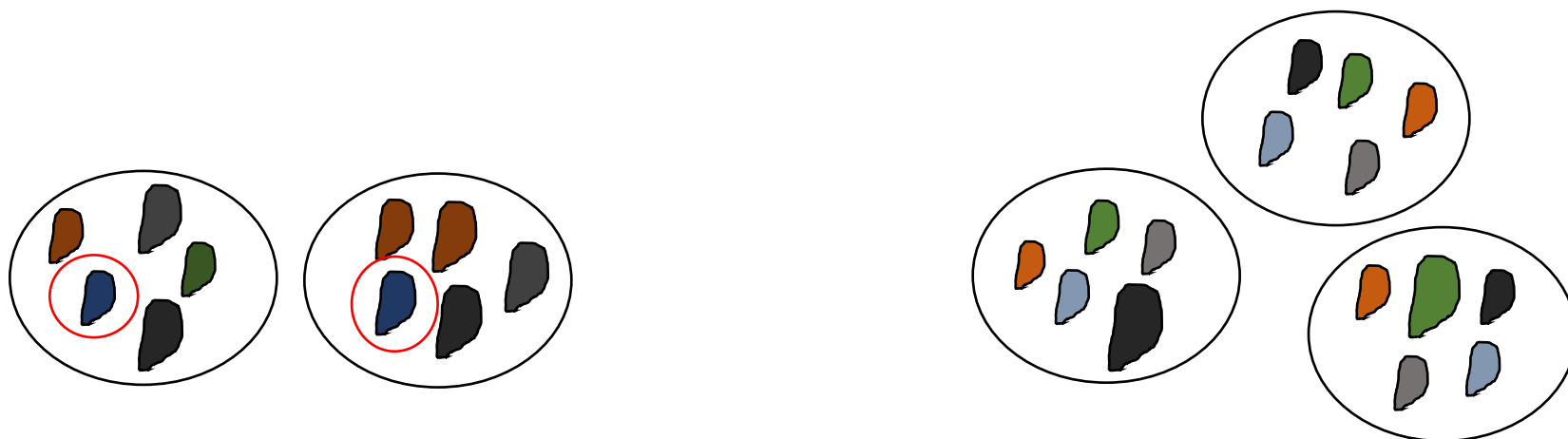


GENETSKA RAZNOLIKOST I GENETSKA DIFERENCIJACIJA



Genetski markeri?

- mitohondrijska DNA (16S, COI)
- alozimi (različiti izozimi istog proteina)
- mikrosateliti (ponavljajući tandem $(ACA)_n$)
- AFLP (fragmenti DNA različite dužine dobiveni digestijom enzima)
- SNPs (varijabilni pojedinačni nukleotidi, npr, A ili T)
- eksprimirani geni (mRNA) - transkriptomika

GENETSKI MARKERI?

- rata mutacije (mtDNA niska, mikrosateliti i SNP-ovi visoka)
- neutralni ili pod utjecajem selekcije (oni koji utječu na gensku ekspresiju)
- cijena – novac, vrijeme ili **znanje**
- broj – rašireni po genomu (SNP-ovi) ili samo lokalizirano, o broju ovisi i statistička snaga
- razvoj novih markera i specifičnost

GENETSKA RAZNOLIKOST mjeri se određivanjem npr.:

- broj genetskih varijanti u populaciji (alelno bogatstvo- ukupan broj alela, nukelotidna raznolikost)
- heterozigotnost (AA, AB, BB)
- privatni aleli – aleli prisutni samo u određenoj populaciji

VAŽNOST GENETSKE RAZNOLIKOSTI

- genetska raznolikost omogućuje **dovoljno varijabilnosti u genomu za djelovanje selekcije u novim okolišnim uvjetima**, i stoga je neophodna za adaptivnu evoluciju
 - smanjen fitnes zbog **razmnožavanja u srodstvu** (inbreeding depression) posljedica je smanjenja genetske raznolikosti i **mutacijskog opterećenja** (povećan broj štetnih mutacija u populaciji)
- za održavanje genetske raznolikosti ključni su **veličina populacije i protok gena**

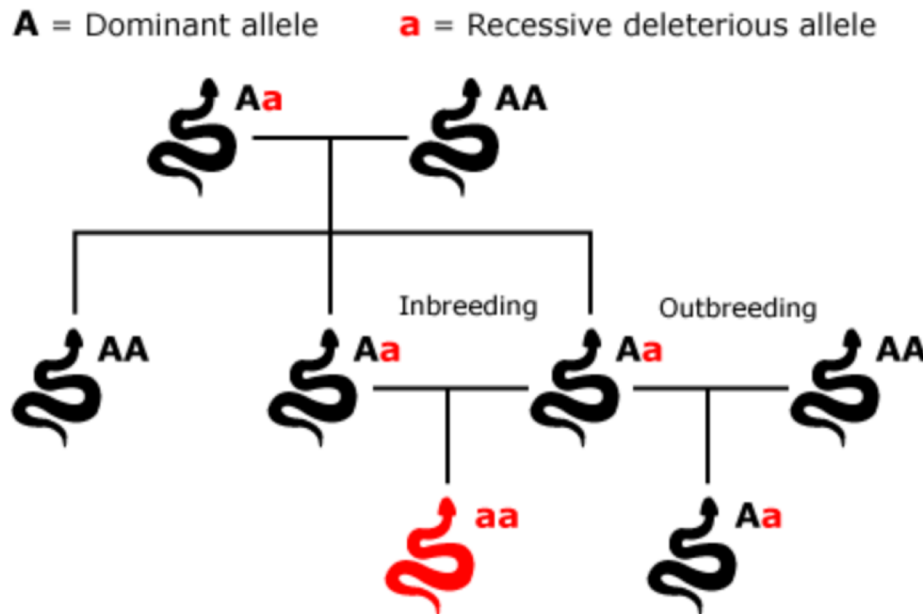


**Zeleni mostovi ili prijelazi za
divlje životinje – omogućavaju
protok gena**



- **Razmnožavanje u srodstvu** (inbreeding depression) ima za posljedicu smanjeno preživljavanje i fertilitet potomaka. Učinci su zabilježeni kod biljaka, životinja i ljudi.
- **Štetne mutacije** (uglavnom recesivne) koje su prisutne u niskoj frekvenciji u populaciji povećavaju učestalost kod razmnožavanja u srodstvu, odnosno dolazi do povećanog broja jedinki koji ispoljuju njihov utjecaj (AA, Aa, aa)
- Razmnožavanje u srodstvu **isto smanjuje broj heterozigota** za svojstva koja su pod utjecajem balansirajuće selekcije, pa se vidi smanjeni fitness homozigota (AA, Aa, aa)

- 40 riđovki (*Vipera berus*) su u Švedskoj izolirane od drugih populacija uslijed poljoprivrednih djelatnosti
- Zabilježena je visoka učestalost mrtvorodenih i deformiranih mladih zmijica (31.6%)
- Nakon što je 1992 u populaciju unešeno 20 novih mužjaka iz dviju drugih populacija (eng. outbreeding) izolirana populacija se oporavila i imala visok broj zdravih potomaka
- Nedostatak nevijabilnih potomaka objašnjava se intra uterinom selekcijom sperme optimalnih haplotipova mužjaka (*cryptic female choice*)



Genetsko spašavanje!!

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

GONZALO ÁLVAREZ¹, FRANCISCO C. CEBALLOS*¹ and TIM M. BERRA FLS^{2,3}

Analiza broja potomaka po ženi pokazuje znatne štetne učinke razmnožavanja u srodstvu u muškoj liniji

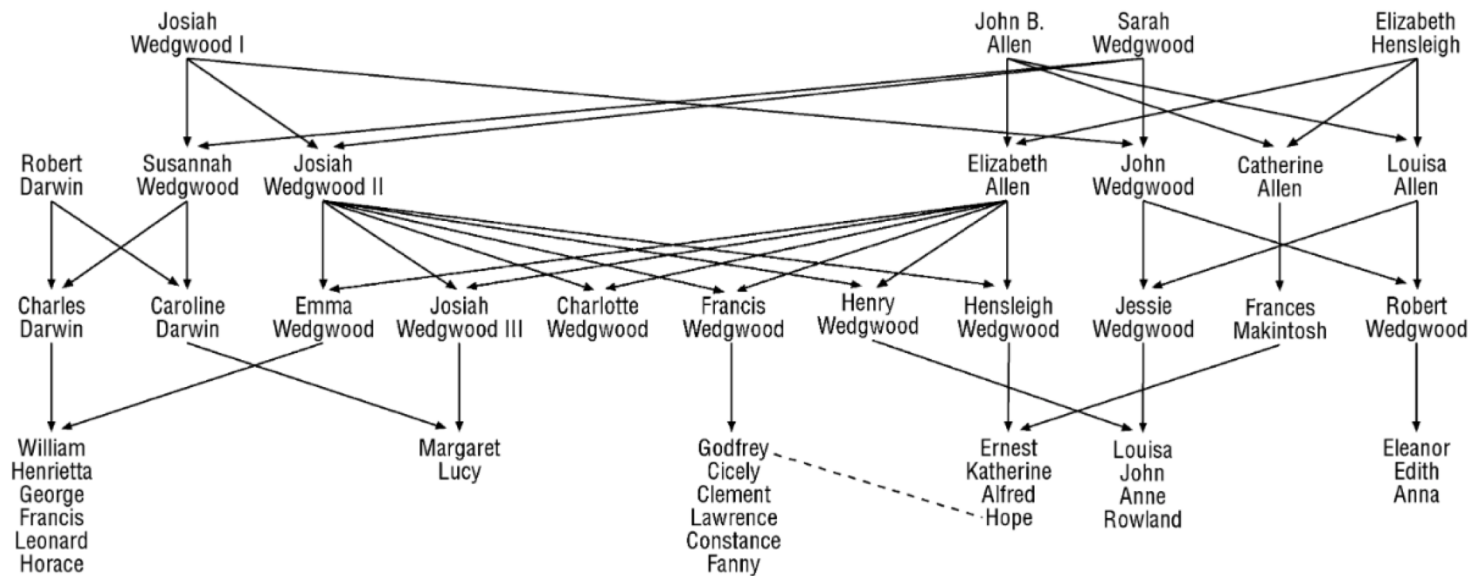


Figure 1. Partial pedigree of the 26 individuals of the Darwin–Wedgwood dynasty considered for the fertility analysis.

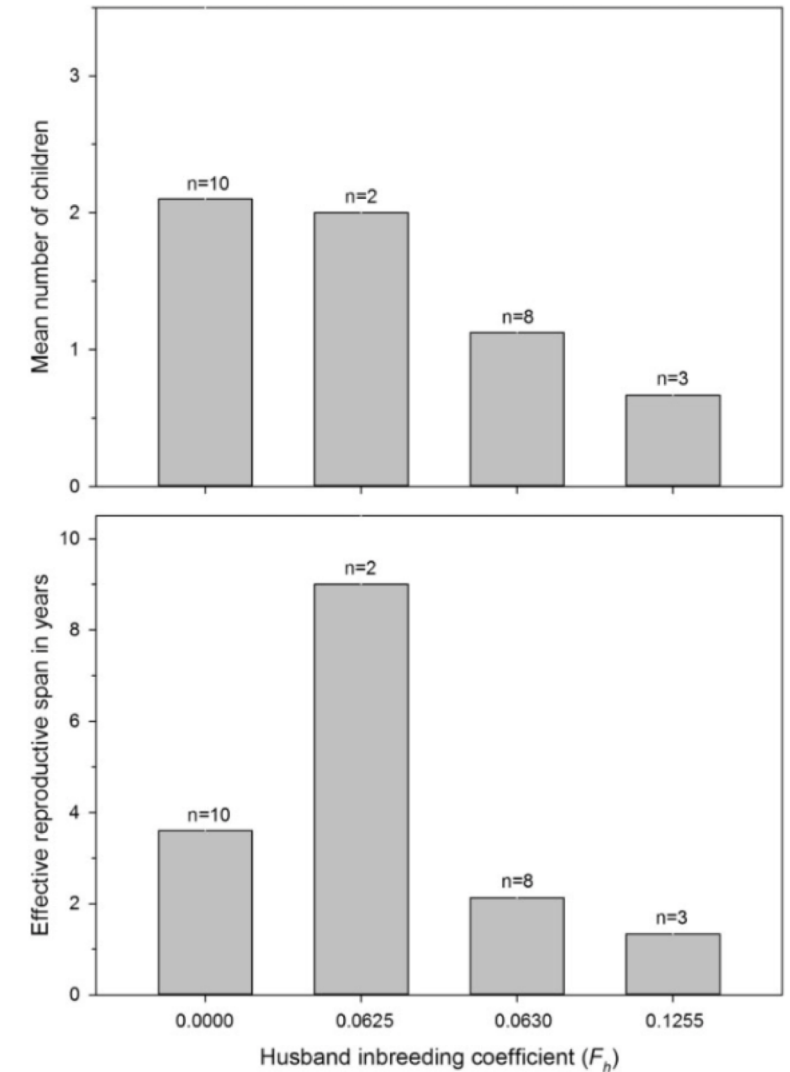
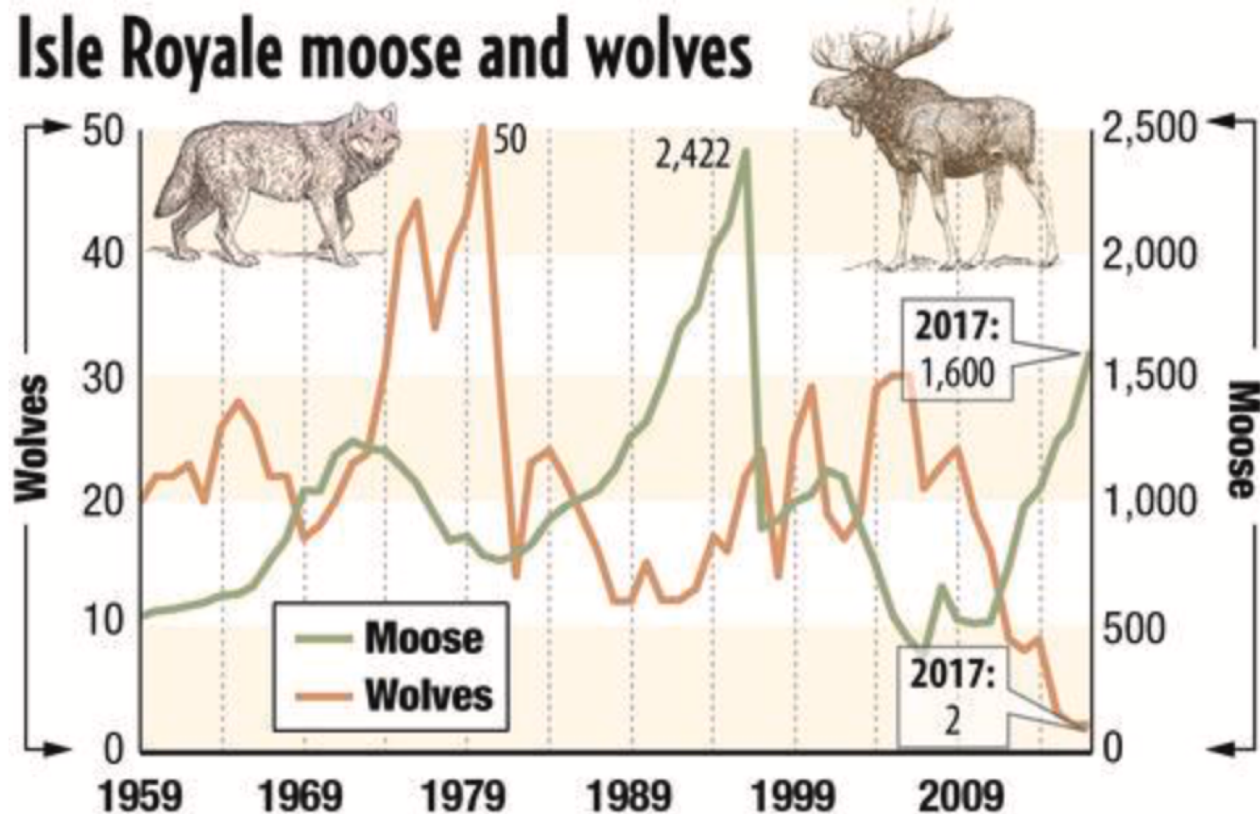


Figure 2. Mean number of children and effective reproductive span for different values of husband inbreeding coefficient (F_h) from 23 Darwin–Wedgwood marriages. The bars corresponding to $F_h = 0.0630$ represent fertility values for Charles Darwin’s son.

- Populacija vukova na otočiću Royale osnovana je 50- tih godina 20. stoljeća vukovima s kopna.
- 1980. g. unešen virus od posjetiteljevog psa – visoki mortalitet.
- Mužjak vuka *M93* migrirao je na otočić s kanadskog kopna 1997. g.
- *M93* je bio vrlo dominantan u odnosu na rezidentne mužjake, razmnožava se s većinom ženki na otoku te njegovi potomci nasljeđuju to svojstvo
- Njegovi potomci u 2008. g. čine 59,4% genetske pozadine populacije
- Populacija vukova pada u brojnosti – u 2012 i 2013 na samo 9 i 8 vukova; u 2018 ostaje ih samo dvoje
- U 2018. g. introducirani vukovi sa susjednog otočića i s kopna
- Preživjeli su samo vukovi introducirani s otočića

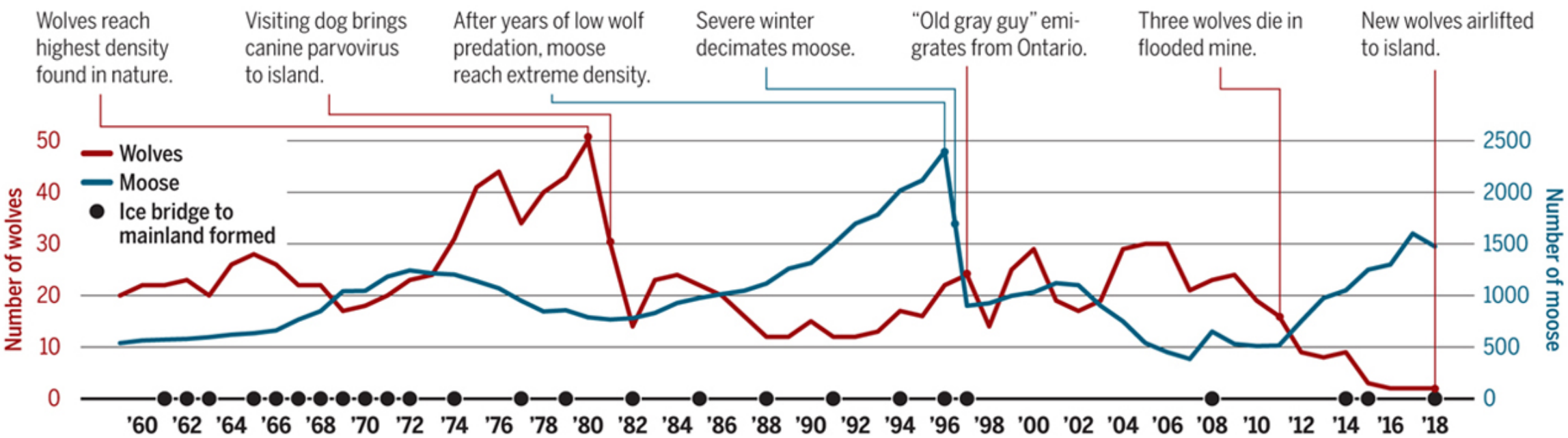




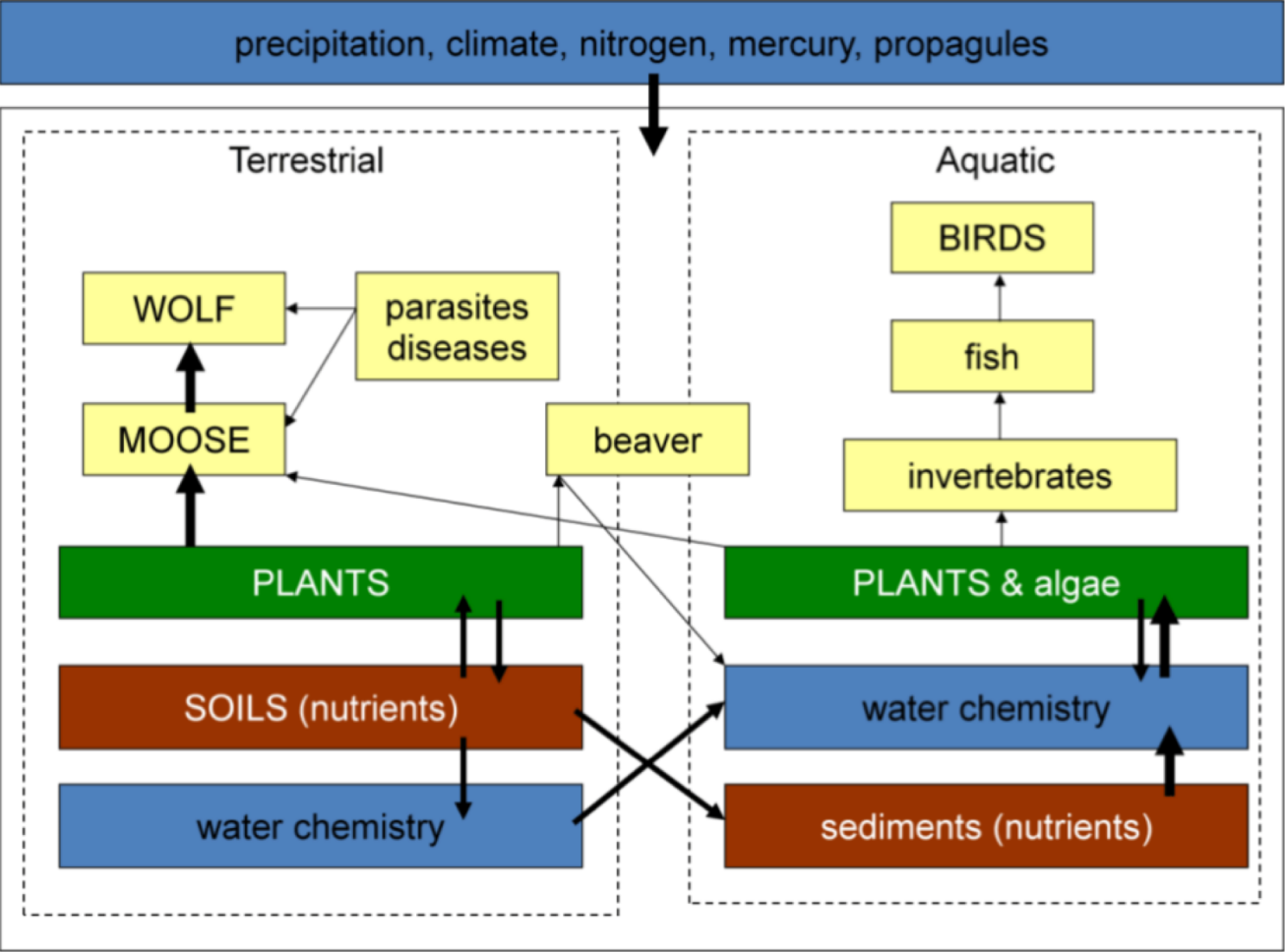
„A 2009 paper in *Biological Conservation* reported that 58% of examined wolves had congenital spinal deformities, compared with only 1% of wolves in other populations. ”

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.



Introducirati ili ne?



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

Ovo nije genetsko spašavanje, već genetsko zamjenjivanje! (not genetic rescue, but genetic replacement!)

EVOLUTIONARY BIOLOGY

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

Jacqueline A. Robinson^{1*†}, Jannikke Räikkönen², Leah M. Vucetich³, John A. Vucetich³, Rolf O. Peterson³, 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.

- genetski drift

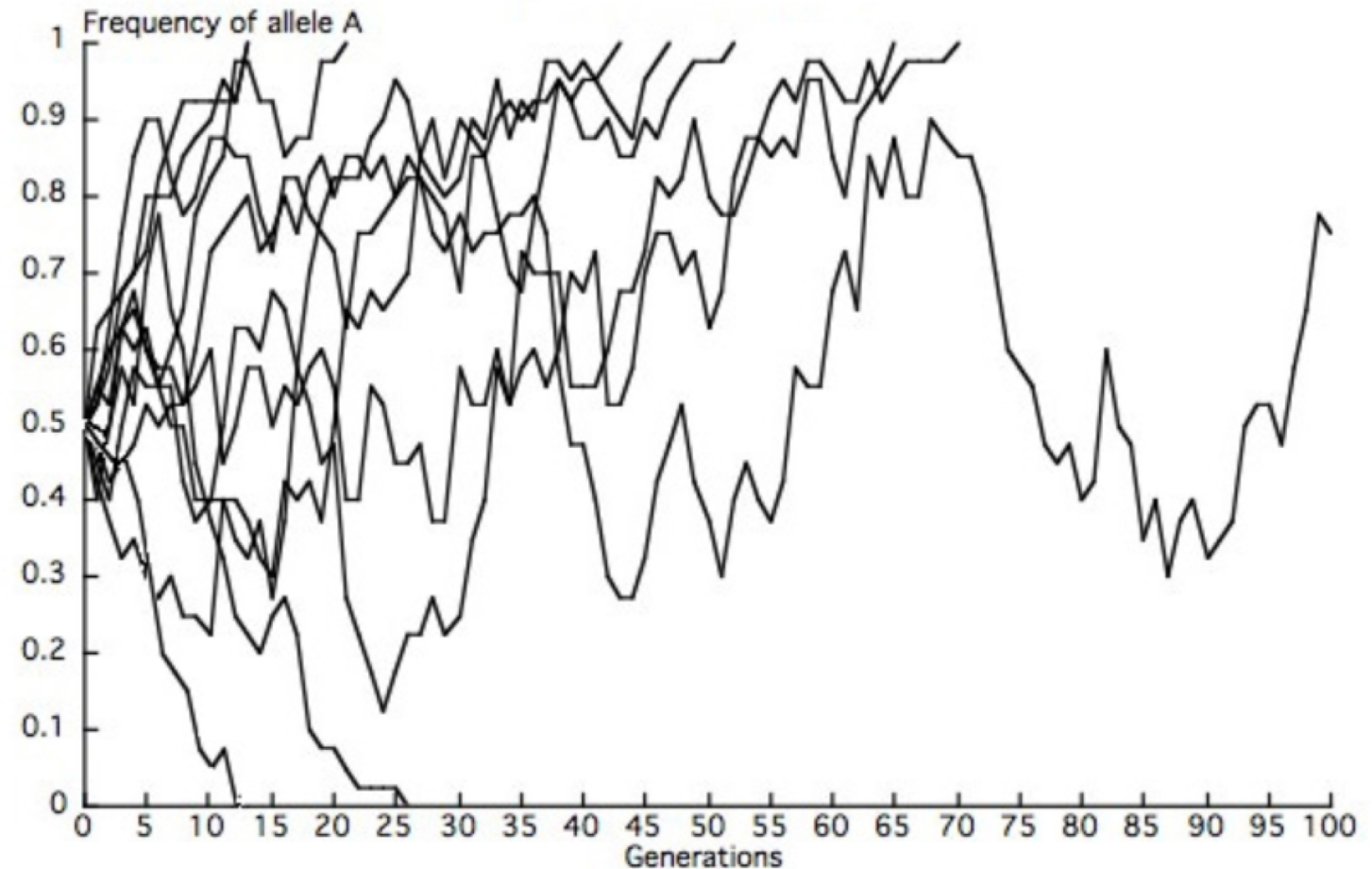


Figure 2: Simulations of allele-frequency change in 10 replicate populations ($N = 20$)

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.

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GENOMSKA DIFERENCIJACIJA

RAD TAGS

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

SNPs

➤ *≈ više tisuća SNP-ova po jedinci*

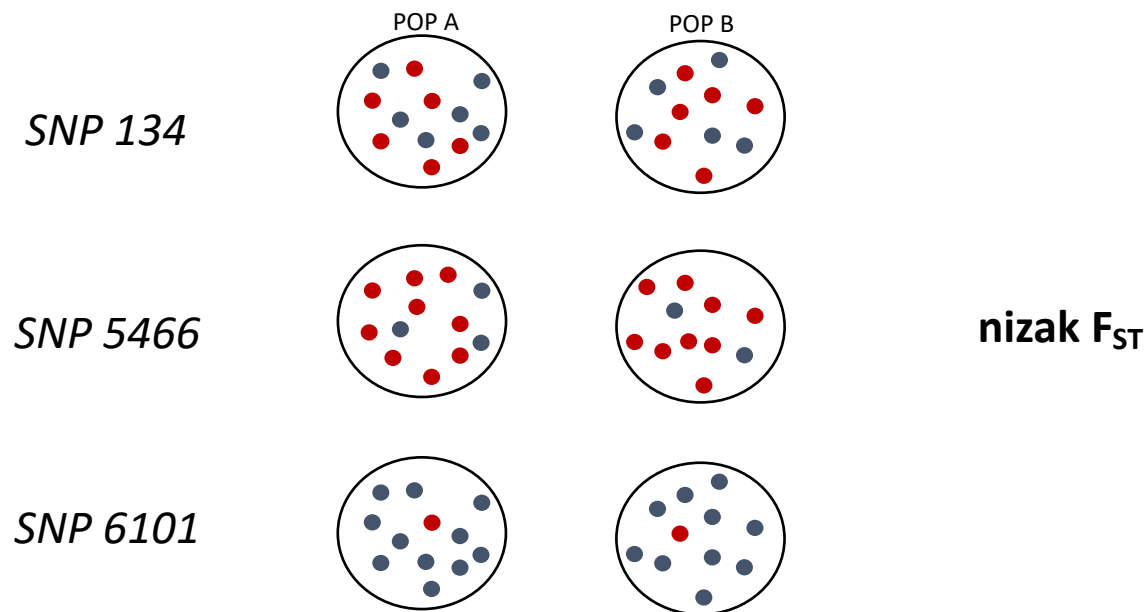
RAD TAGS

DAAN	ACTGGC A GCGAATCTAGTGCGTAA
LOTTE	ACTGGC C GCGAATCTAGTGCGTAA
LEVI	ACTGGC C GCGAATCTAGTGCGTAA
LISA	ACTGGC A GCGAATCTAGTGCGTAA
EMMA	ACTGGC C GCGAATCTAGTGCGTAA
SEM	ACTGGC A GCGAATCTAGTGCGTAA

SNPs

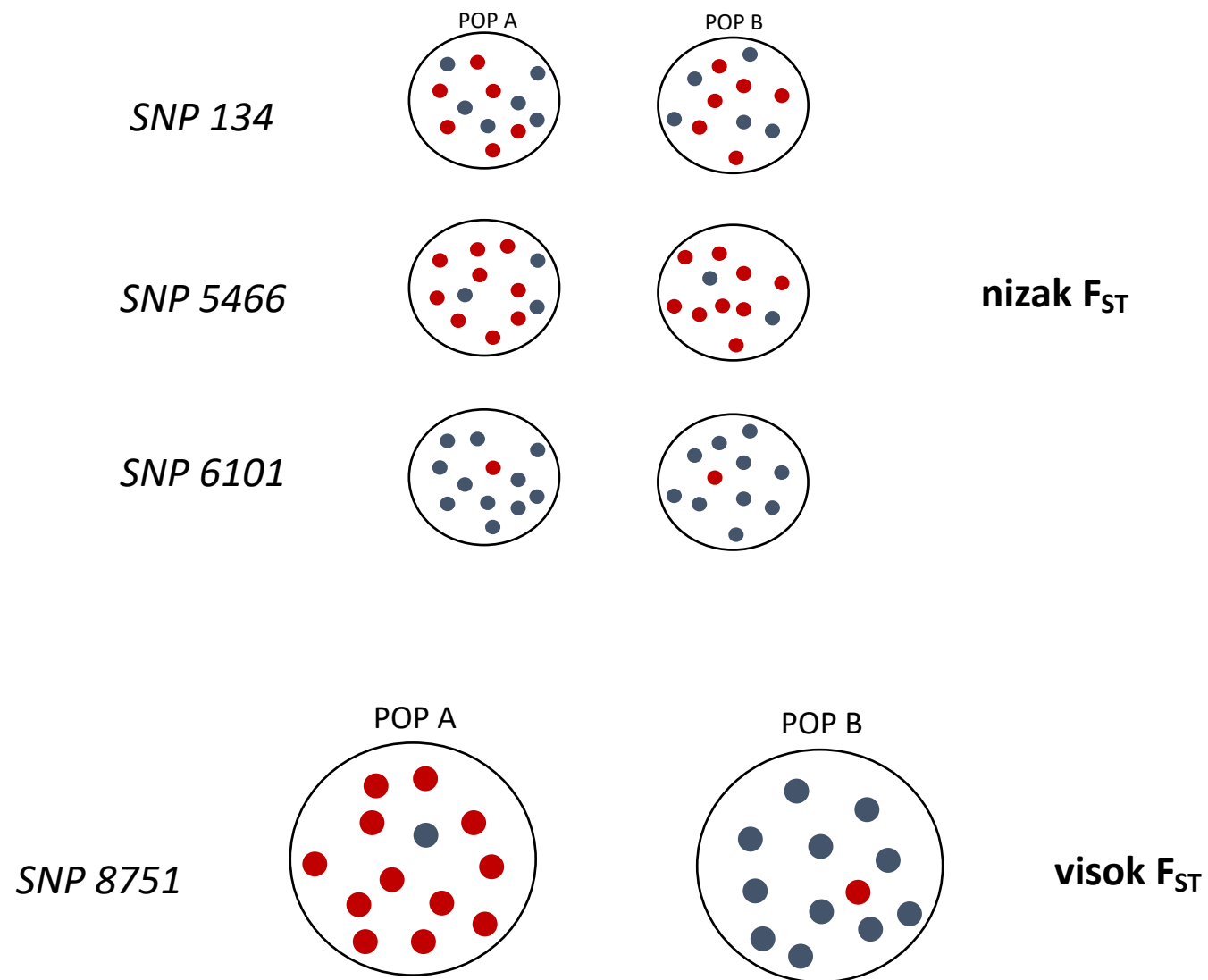
➤ *≈ više tisuća SNP-ova po jedinci*

LOKUS F_{ST}



F_{ST} je fiksacijski indeks, usporedba genetičke varijabilnosti između populacija s genetičkom varijabilnosti unutar populacija

LOKUS F_{ST}



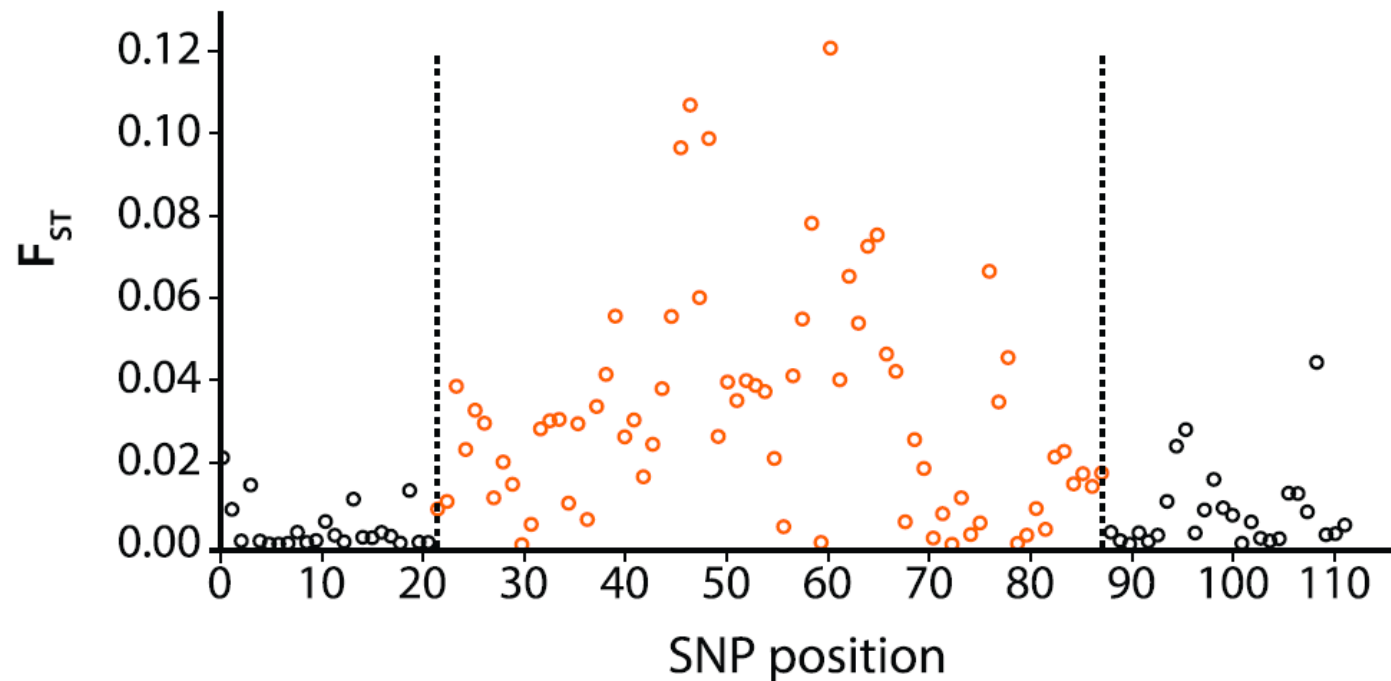
- F_{ST} možemo mjeriti po lokusu i preko svih genomskih markera
- F_{ST} srednja vrijednost za sve markere nam daje uvid u diferencijaciju populacija

		Bulgarians	Macedonians	Montenegrins	Serbians	Bosnians	Croatians	Slovenias	Czechs	Slovaks	Sorbs	Poles	Ukrainians	Belarusians	Russians South	Russians Central	Russians North	Lithuanians	Latvians
Bulgarians		0.0000	0.0000	0.0014	0.0000	0.0007	0.0007	0.0012	0.0019	0.0016	0.0043	0.0030	0.0023	0.0033	0.0030	0.0045	0.0124	0.0058	0.0059
Macedonians		0.0000	0.0000	0.0017	0.0004	0.0007	0.0007	0.0013	0.0017	0.0021	0.0045	0.0031	0.0025	0.0031	0.0032	0.0048	0.0127	0.0065	0.0066
Montenegrins		0.0014	0.0017	0.0000	0.0007	0.0017	0.0018	0.0021	0.0033	0.0030	0.0055	0.0043	0.0034	0.0048	0.0044	0.0056	0.0145	0.0077	0.0073
Serbians		0.0000	0.0004	0.0007	0.0000	0.0003	0.0002	0.0013	0.0012	0.0012	0.0043	0.0023	0.0019	0.0025	0.0025	0.0036	0.0119	0.0052	0.0054
Bosnians		0.0007	0.0007	0.0017	0.0003	0.0000	0.0001	0.0008	0.0008	0.0010	0.0035	0.0017	0.0013	0.0022	0.0018	0.0030	0.0108	0.0042	0.0038
Croatians		0.0007	0.0007	0.0018	0.0002	0.0001	0.0000	0.0004	0.0004	0.0008	0.0028	0.0013	0.0010	0.0016	0.0014	0.0024	0.0109	0.0036	0.0036
Slovenians		0.0012	0.0013	0.0021	0.0013	0.0008	0.0004	0.0000	0.0011	0.0008	0.0029	0.0015	0.0009	0.0014	0.0015	0.0028	0.0110	0.0042	0.0037
Czechs		0.0019	0.0017	0.0033	0.0012	0.0008	0.0004	0.0011	0.0000	0.0004	0.0021	0.0005	0.0007	0.0011	0.0009	0.0021	0.0101	0.0026	0.0029
Slovaks		0.0016	0.0021	0.0030	0.0012	0.0010	0.0008	0.0008	0.0004	0.0000	0.0026	0.0006	0.0007	0.0012	0.0012	0.0018	0.0098	0.0030	0.0026
Sorbs		0.0043	0.0045	0.0055	0.0043	0.0035	0.0028	0.0029	0.0021	0.0026	0.0000	0.0022	0.0021	0.0023	0.0026	0.0035	0.0110	0.0039	0.0036
Poles		0.0030	0.0031	0.0043	0.0023	0.0017	0.0013	0.0015	0.0005	0.0006	0.0022	0.0000	0.0002	0.0000	0.0004	0.0010	0.0087	0.0011	0.0011
Ukrainians		0.0023	0.0025	0.0034	0.0019	0.0013	0.0010	0.0009	0.0007	0.0007	0.0021	0.0002	0.0000	0.0003	0.0006	0.0012	0.0089	0.0020	0.0019
Belarusians		0.0033	0.0031	0.0048	0.0025	0.0022	0.0016	0.0014	0.0011	0.0012	0.0023	0.0000	0.0003	0.0000	0.0005	0.0012	0.0089	0.0008	0.0015
Russians South		0.0030	0.0032	0.0044	0.0025	0.0018	0.0014	0.0015	0.0009	0.0012	0.0026	0.0004	0.0006	0.0005	0.0000	0.0008	0.0086	0.0022	0.0018
Russians Central		0.0045	0.0048	0.0056	0.0036	0.0030	0.0024	0.0028	0.0021	0.0018	0.0035	0.0010	0.0012	0.0012	0.0008	0.0000	0.0059	0.0021	0.0014
Russians North		0.0124	0.0127	0.0145	0.0119	0.0108	0.0109	0.0110	0.0101	0.0098	0.0110	0.0087	0.0089	0.0089	0.0086	0.0059	0.0000	0.0098	0.0096
Lithuanians		0.0058	0.0065	0.0077	0.0052	0.0042	0.0036	0.0042	0.0026	0.0030	0.0039	0.0011	0.0020	0.0008	0.0022	0.0021	0.0098	0.0000	0.0000
Latvians		0.0059	0.0066	0.0073	0.0054	0.0038	0.0036	0.0037	0.0029	0.0026	0.0036	0.0011	0.0019	0.0015	0.0018	0.0014	0.0096	0.0000	0.0000

F_{ST} genetic distances between Slavic speakers in the Balkans and Slavic speakers in East Europe – slika je s Twittera i samo je ilustrativna!

F_{ST} OUTLIERI

LOKUSI POD DJELOVANJEM SELEKCIJE



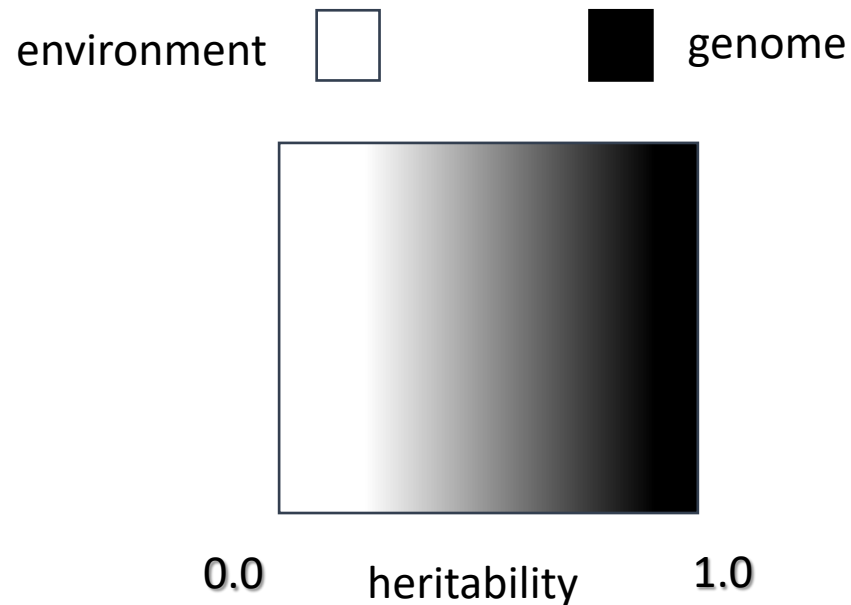
GENOMSKA OSNOVA ADAPTACIJE

Nasljednost, genetska arhitektura i glavne genetske interakcije

- nasljednost (heritability)
- aditivna genetska varijacija (additive genetic variation)
- epistaza
- pleiotropija
- “trade off”

Nasljednost (HERITABILITY) je koncept koji sumarno gleda koliko **varijabilnosti** u fenotipskom svojstvu potječe od genetskih čimbenika.

NASLJEDNOST NIJE UDIO FENOTIPA KOJI JE POD UTJECAJEM GENETSKIH ČIMBENIKA!!!



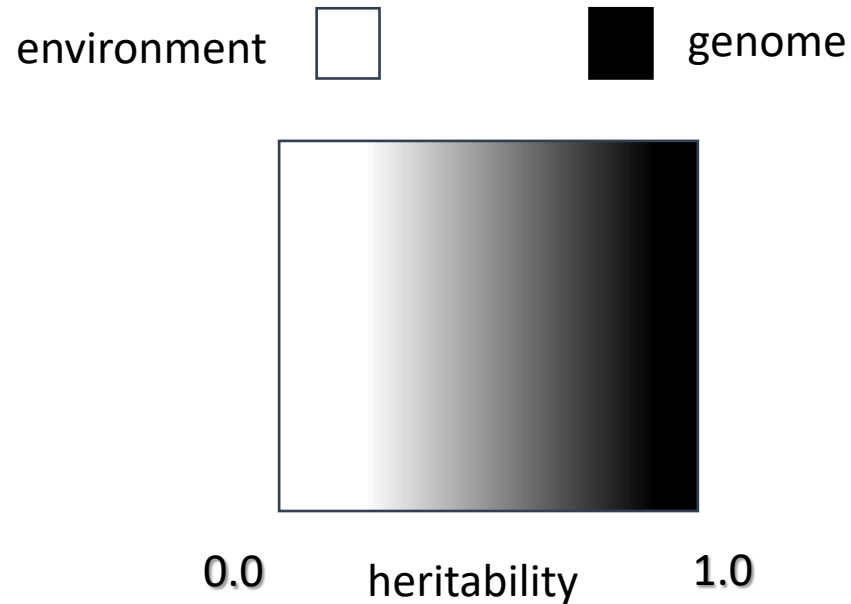
Procjena nasljednosti nekog fenotipskog svojstva **specifična je za populaciju u jednom okolišu**, i može se mijenjati kroz vrijeme, u skladu s mijenjanjem ekoloških čimbenika. Vrijednost nasljednosti je u rasponu od 0 do 1. Vrijednost blizu nule označuje da sva **varijabilnost u fenotipu među jednikama** potječe od okoliša, s malim učinkom genetičkih čimbenika.

Nasljednost se uvijek odnosi na varijancu u distribuciji.

NATURE OR NURTURE

Nasljednost (HERITABILITY) je koncept koji sumarno gleda koliko **varijabilnosti** u fenotipskom svojstvu potječe od genetskih čimbenika.

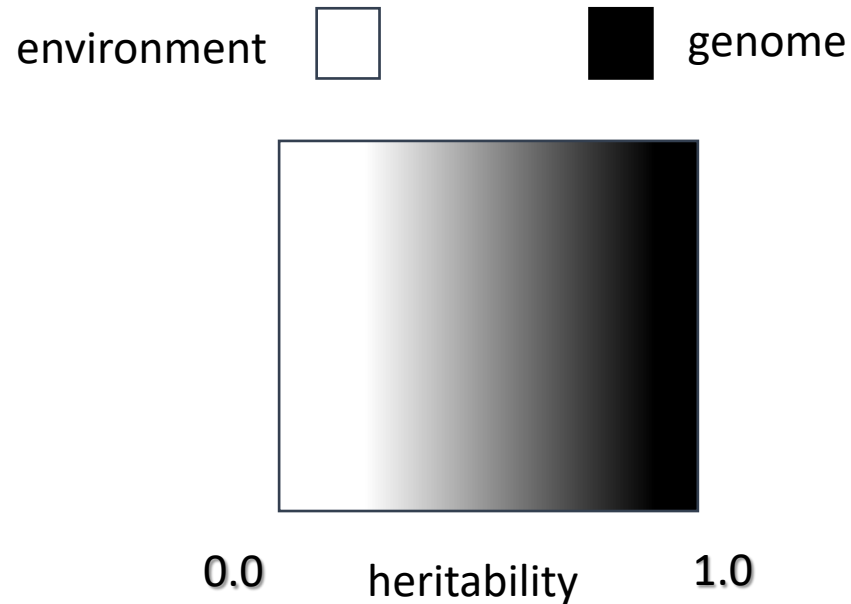
NASLJEDNOST NIJE UDIO FENOTIPA KOJI JE POD UTJECAJEM GENETSKIH ČIMBENIKA!!!



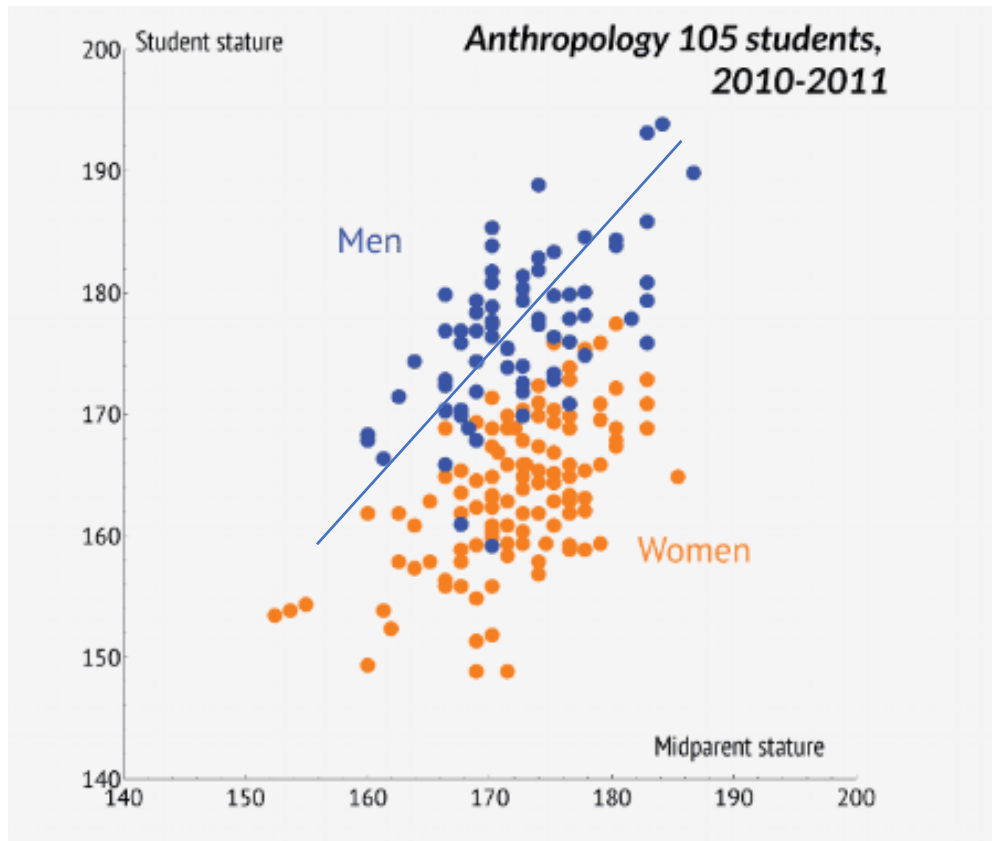
Svojstva pod jakim utjecajem izravne selekcije mogu imati vrlo nisku varijabilnost genotipa u populaciji, i bez obzira što je njihova srednja vrijednost u velikoj mjeri određena genotipom, pokazuju malu nasljednost, jer ukoliko su svi genotipovi jednaki zbog jake selekcije, nema više varijabilnosti zbog genotipa (npr često svojstva izravno vezana uz fitness, primjer: broj udova...).

Nasljednost (HERITABILITY) je koncept koji sumarno gleda koliko **varijabilnosti** u fenotipskom svojstvu potječe od genetskih čimbenika.

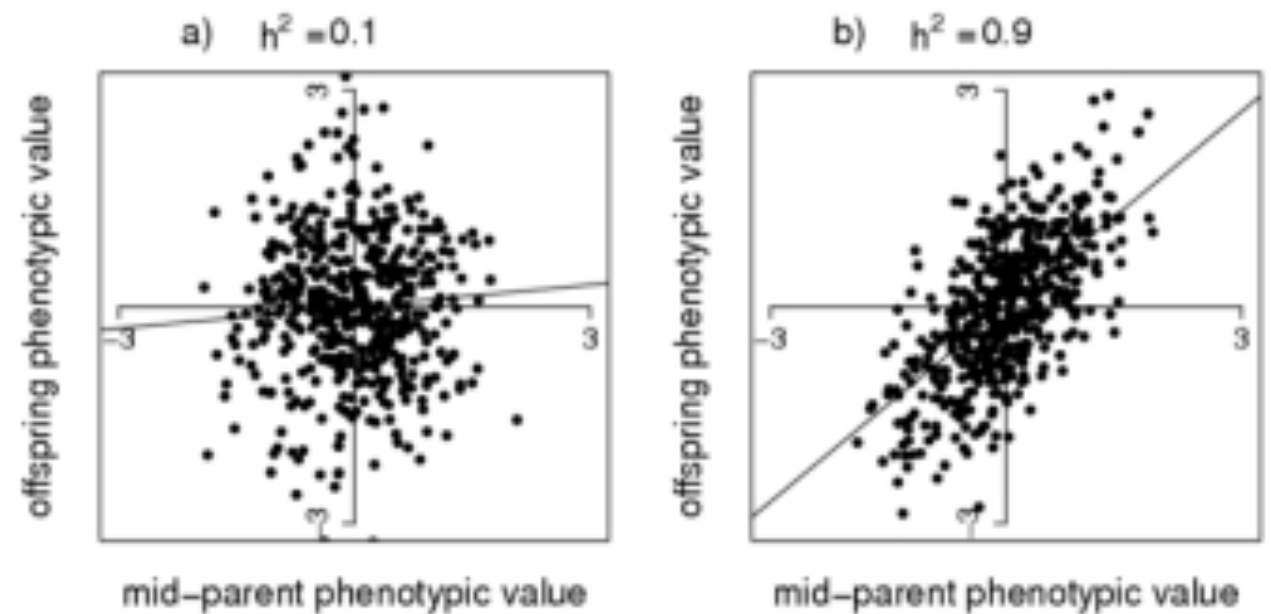
NASLJEDNOST NIJE UDIO FENOTIPA KOJI JE POD UTJECAJEM GENETSKIH ČIMBENIKA!!!



Sama nasljednost nam ne govori koliko je samo svojstvo pod utjecajem gena, nego njegova varijabilnost!!!!

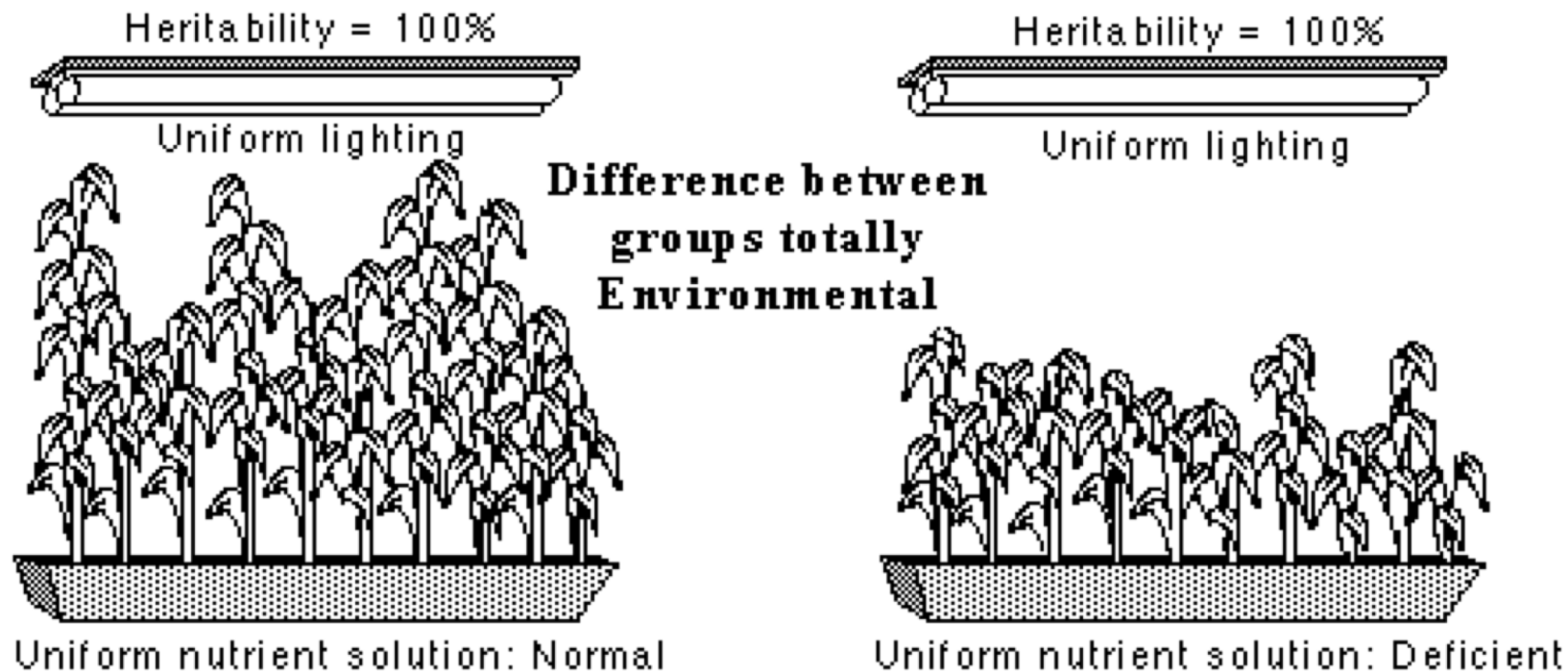


Nasljednost se najlakše izračunava
korelacijom fenotipskog svojstva kod
roditelja i potomaka



1969 Arthur Jensen “How much can we boost IQ and scholastic achievement? – rasizam – razliku u IQ među „rasama” pripisuje genima i nasljednosti

1970 Lewontin – opovrgnuo pretpostavke – nature or nurture



Genetska varijance može biti aditivna i ne-aditivna.

ADITIVNA GENETSKA VARIJANCA- aleli čiji je utjecaj na svojstvo neovisan od okoliša i drugih gena.

aa ab bb

NE-ADITIVNA GENETSKA VARIJANCA- svi nelinearni genetski učinci:

- **dominantnost** (kada prisutnost jednog alela ima jednaki učinak kao dva takva ista alela)
AA Aa aa
- **epistaza** (interaktivni utjecaji različitih gena, utjecaj jednog gena ovisi o utjecaju drugog gena)
- **genetsko-okolišna interakcija** (utjecaj alela mijenja se ovisno o okolišu)

Dio varijance koju objašnjava aditivni genetski učinci zove se **nasljednost u užem smislu**, dok **nasljednost u širem smislu** označava sve genetske učinke.

- evolucija fenotipskog svojstva ovisi o (aditivnoj) genetskoj varijaciji

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Research



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

Parenting behaviour is highly heritable in male stickleback

Alison M. Bell^{1,2,3,4,5}, Rebecca Trapp¹ and

Jason Keagy^{1,2,3,4,5}

<https://youtu.be/f0natXGHyNw>

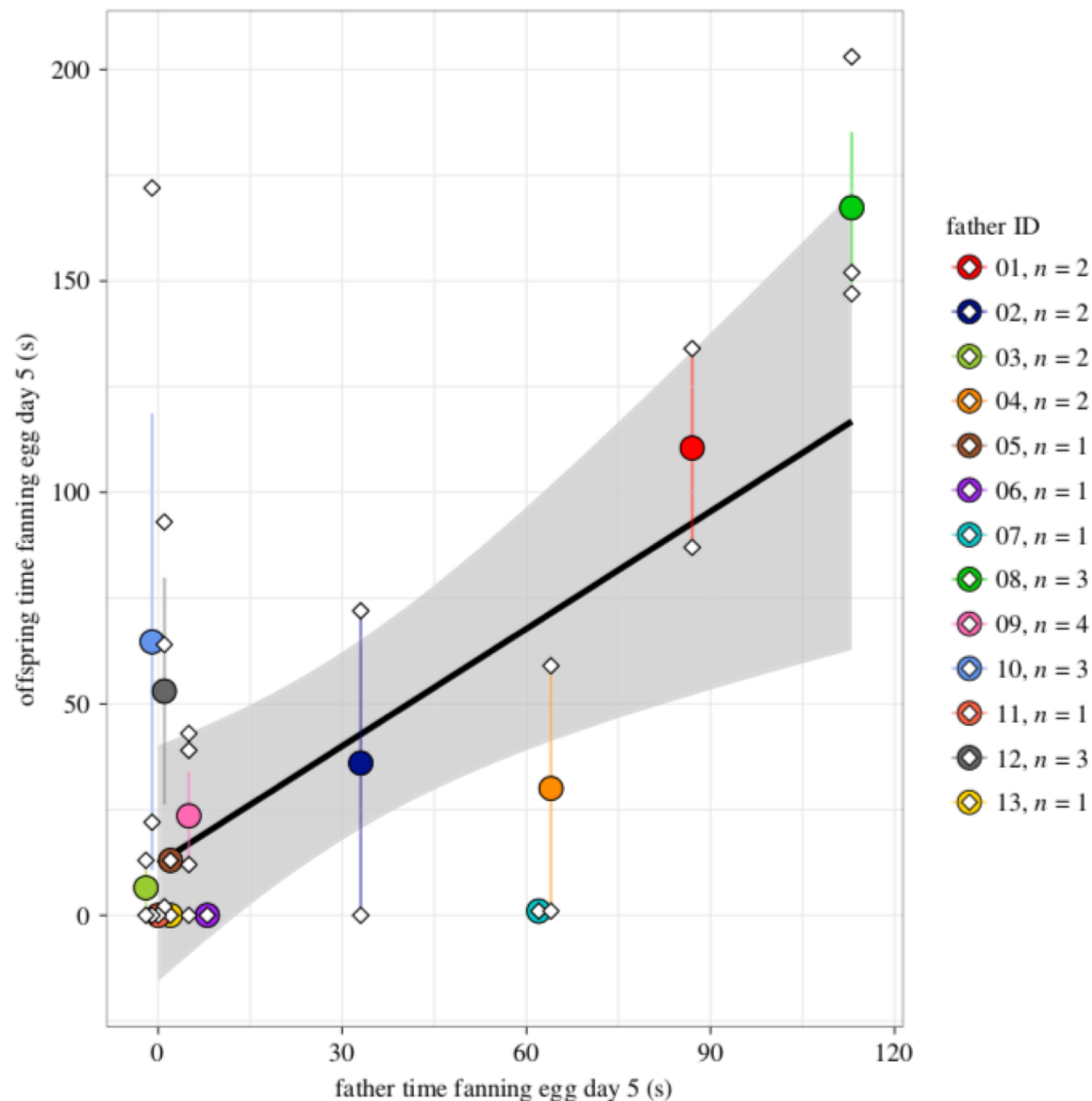


Figure 2. Relationship between fanning in fathers and sons. Son fanning time plotted against father fanning time. For visualization, the regression line is in black and 95% CI are indicated in grey (linear regression: $\beta = 0.92 \pm 0.27$, $t_{11} = 3.48$, $p = 0.005$). Solid circles and lines indicate means $\pm$ 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.

- Nasljednost blizu 1 sugerira vrlo jednostavnu genetsku podlogu
- Teorija predviđa da svojstva pod slabim utjecajem selekcije imaju višu nasljednost, jer se kod svojstva pod jakim utjecajem selekcije smanjuje genetska varijabilnost
- niža selekcija jer se eksprimira samo kod mužjaka
- roditeljsko ponašanje primjer je za neizravne genetske učinke, jer su svojstva jedne jedinke pod utjecajem gena druge jedinke
- visoka nasljednost roditeljskog ponašanja može imati vezu sa seksualnom selekcijom

vrijeme provedeno u brizi o gnijezdu
(*fanning*) očeva i sinova

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



Evolucijski potencijal bilo kojeg svojstva u bilo kojoj populaciji ovisi o genetskoj raznolikosti!

- **Fenotipsko svojstvo mora genetski korelirati s fitnessom da bi evoluirao u odgovoru na prirodnu selekciju, no jaka selekcija smanjuje genetsku varijaciju u fitnessu i smanjuje budući evolucijski potencijal.**

- Fitnes je mjera prinosa gena slijedećoj generaciji kroz procese razmnožavanja i preživljavanja

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

LRS (lifetime reproductive success) – životna reproduktivna uspješnost (veća reproduktivna uspješnost u godinama kada je hrane u izobilju – mast years)

Nasljednost od 0.00049 za LRS

Bilo bi potrebno 275 generacija da se prosječni LRS poveća za jedno mladunče.

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

Susan E. Johnston^{1,2†}, Jacob Gratten^{1,3†}, Camillo Berenos², Jill G. Pilkington², Tim H. Clutton-Brock⁴, Josephine M. Pemberton² & Jon Slate¹

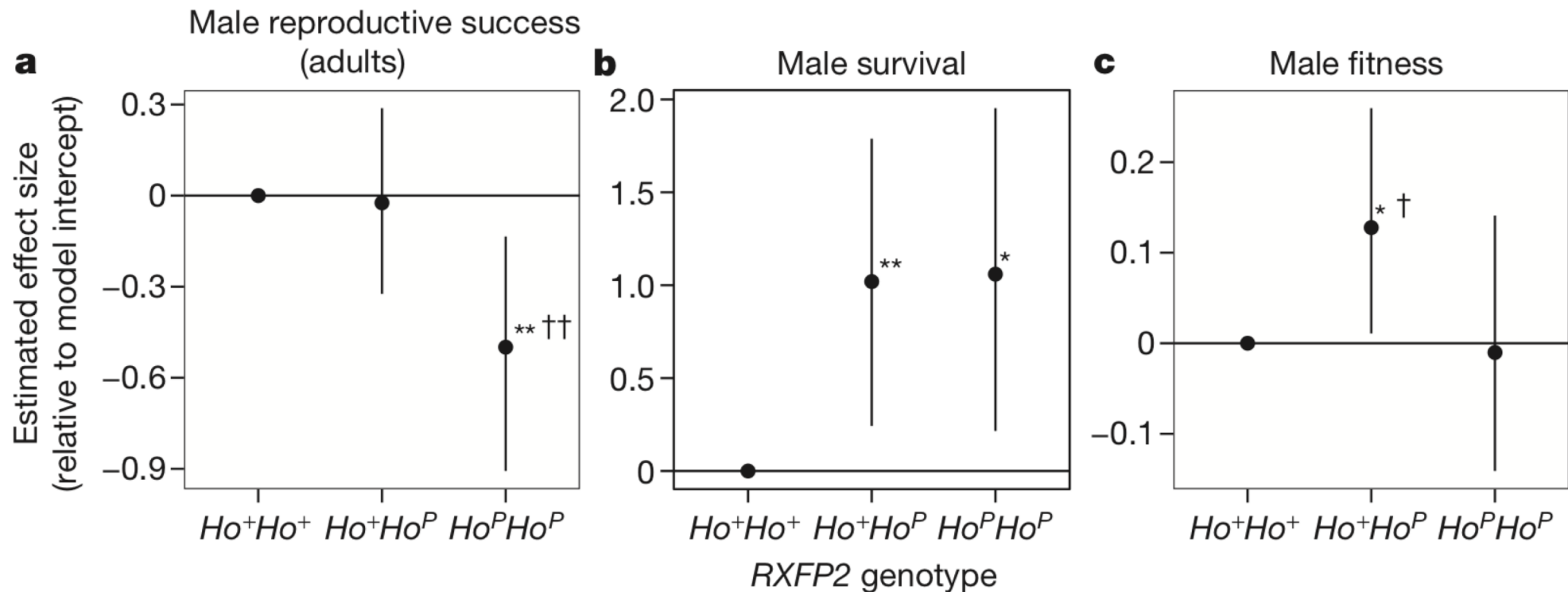
„Trade-off”

veliki rogovi imaju kompetitivnu prednost među mužjacima, i povećava reproduktivnu uspješnost, dok aleli odgovorni za male rogove povećavaju preživljavanje – heterozigoti imaju najveći fitnes



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^PHo^P . **d**, Three-year-old scurred Ho^PHo^P .

„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 size⁶. 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, $Ho1$, is associated with **higher reproductive success**, whereas a smaller horn allele, HoP , **confers increased survival**, resulting in a net effect of overdominance (that is, **heterozygote advantage**) for fitness at *RXFP2*. „



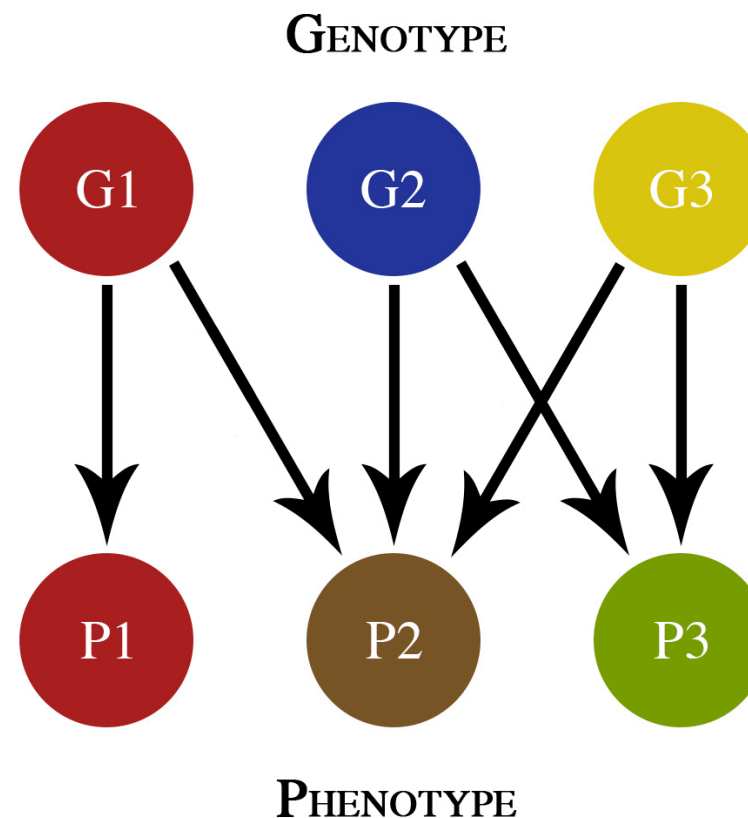
prednost heterozigota!

isti aleli nađeni su kod miša i
čovjeka i povezani su s gustoćom
kostiju i spolnim razvojem

-spolno selektirana svojstva često prelaze točku u kojem su optimalna za preživljavanje, što znači da postoji trade-off između seksualnog i neseksualnog fitnesa

Pleiotropija je svojstvo gena da utječu na multipne funkcije i karakteristike organizma.

Trade off – posebni slučaj pleiotropije kada prinos jednoj funkciji ili svojstvu smanjuje prinos drugoj funkciji ili svojstvu- **antagonistična pleiotropija**



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

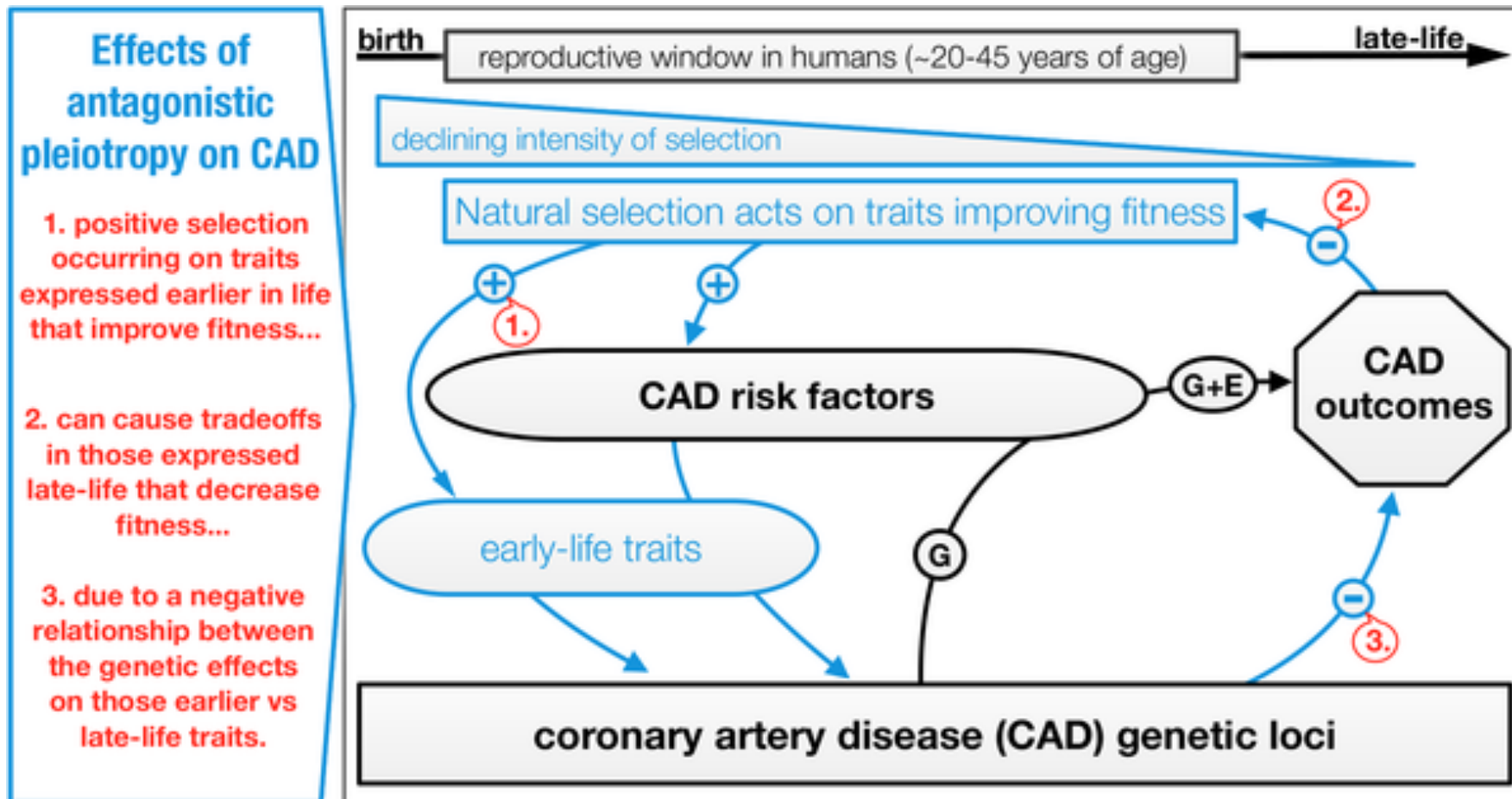
Sean G. Byars , Qin Qin Huang, Lesley-Ann Gray, Andrew Bakshi, Samuli Ripatti, Gad Abraham, Stephen C. Stearns, Michael Inouye 

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

prirodna selekcija
održava alele
odgovorne za razvoj
kardiovaskularnih
bolesti jer imaju utjecaj
na ljudsku reprodukciju

„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].



negativan odnos među genetskim učincima na svojstva u ranoj i kasnoj životnoj dobi

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>

Pleiotropy in the melanocortin system, coloration and behavioural syndromes

Anne-Lyse Ducrest, Laurent Keller and Alexandre Roulin

Kovarijacija obojenosti i ponašanja, fizioloških i morfoloških svojstva pod utjecajem eumelanina kod divljih populacija kralješnjaka

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
Aggressiveness and exocrine gland activity		—	0
	Aggressiveness	+	18
		—	2
Stress response	Mass of uropygial gland	+	0
		—	1
	Resistance to stressors	+	6
Immune system		—	0
	Immune response against nonpathogenic antigen	+	1
		—	0
Energy homeostasis	Metabolic rate	+	2
		—	0
	Body mass	+	7
		—	3
	Body size	+	7
		—	1

^aNumber of studies showing a significant positive or negative correlation between eumelanin-based coloration and other phenotypic attributes.

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.”*

tamnije obojeni kralješnjaci su agresivniji, seksualno aktivniji i otporniji na stres nego svijetlo obojene jedinke-
pleiotropski učinci melanokortina

POMC gen odgovoran je za produkciju melanokortina, koji se veže na 5 različitih receptora u različitim tkivima. Antagonisti melanokortina su ASIP i AGRP proteini, te i oni utječu na njegovo djelovanje u pojedinom tkivu (**epistaza**).

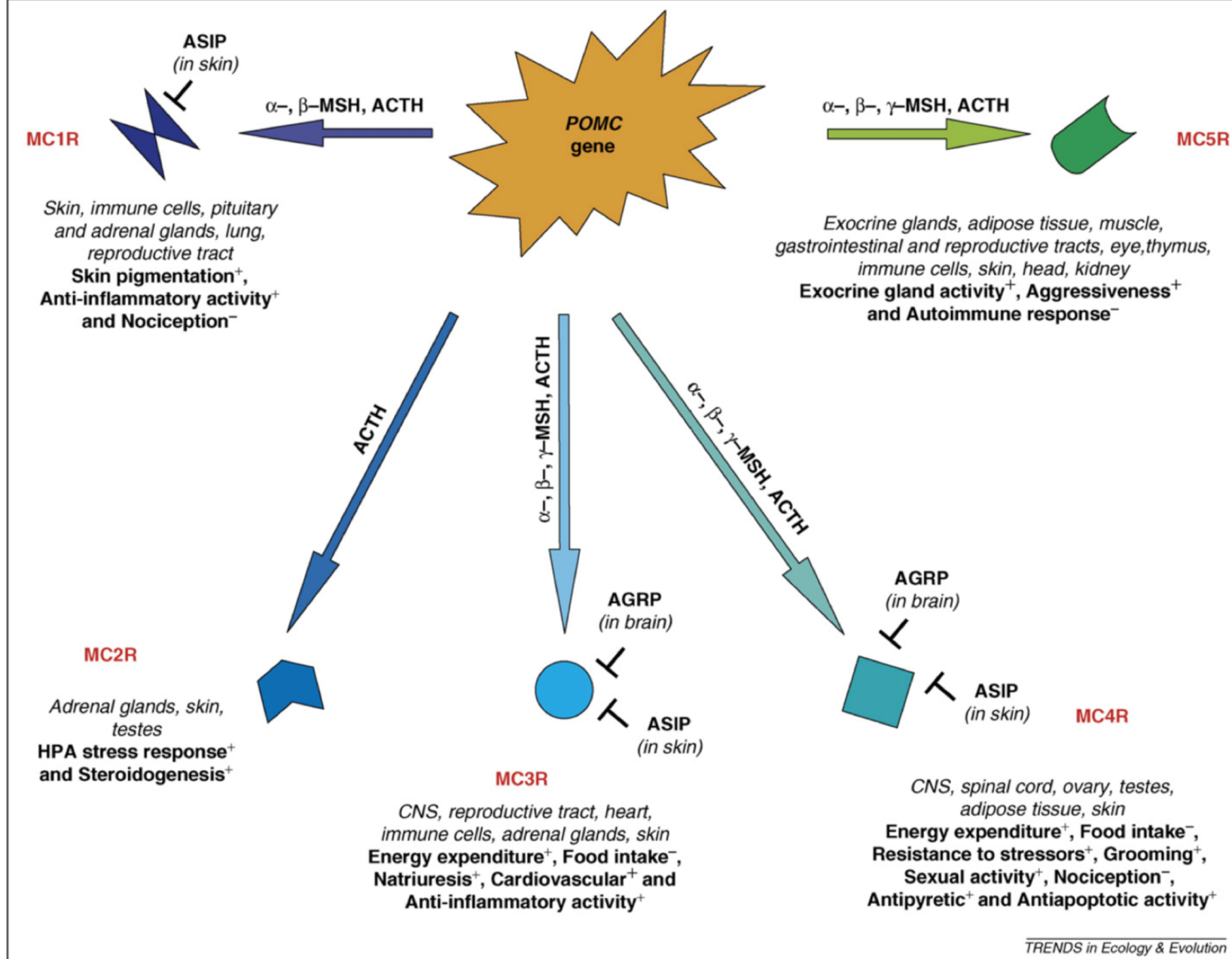


Figure 3. Melanocortin system. The *proopiomelanocortin* (POMC) gene produces the melanocortins (α -, β - and γ -MSH and ACTH) which bind to five melanocortin receptors (MC1–5R). Location of these five receptors in vertebrates is given in italics while their function is written in bold. For each function, 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 $\perp$.

Disease outbreaks select for mate choice and coat color in wolves

SARAH CUBAYNES ^{ID}, ELLEN E. BRANDELL ^{ID}, DANIEL R. STAHLER ^{ID}, DOUGLAS W. SMITH, EMILY S. ALMBERG ^{ID}, SUSANNE SCHINDLER ^{ID}, ROBERT K. WAYNE ^{ID}, ANDREW P. DOBSON ^{ID}, BRIDGETT M. VONHOLDT ^{ID}, [...], AND TIM COULSON ^{ID} [+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

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 population⁴. 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) ERAP2 transcript, **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**”*



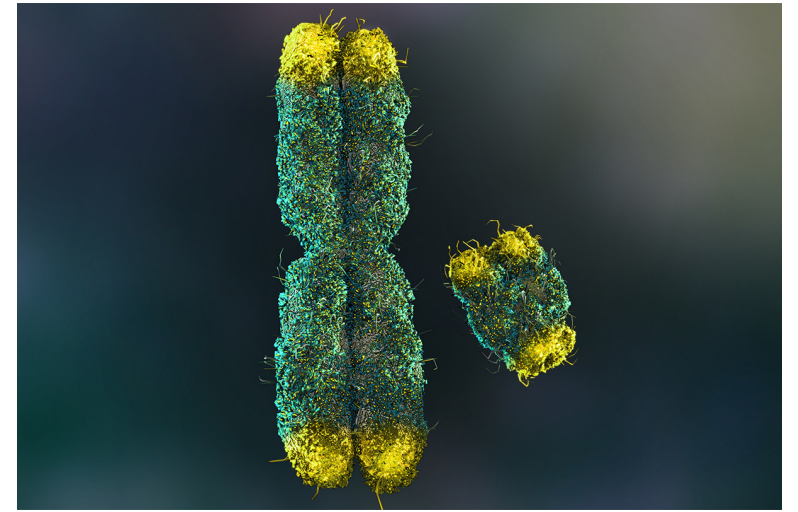
Evolution of Human-Specific Alleles Protecting Cognitive Function of Grandmothers

*“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.”*

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](https://doi.org/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.”

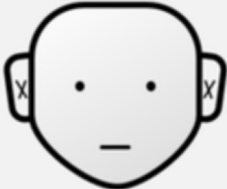
- **Epistaza**
- **Stresni kontekst** (genetski ili okolišni) je situacija u kojem je apsolutni fitnes divljeg tipa smanjen u odnosu na neku drugu situaciju.
- Promjene okoliša- kao smanjenje hrane ili povećanje predatora, izloženost ekstremnim temperaturama ili toksikantima stresne su za većinu organizama.
- Fitnes može biti ugrožen i epistatskim interakcijama među alelima i mutacijama, kada je **fitnes jednog alela pod utjecajem mutacije na drugim lokusima**

a Dominant epistasis (Mendelian)



dominantni alel (*I*) na *KIT* lokusu, koji određuje bijelu boju krzna kod svinja, je dominantan nad svim alelima na *MC1R* lokusu (*E*), koji određuju tamnije boje krzna

geni za ćelavost
dominantni su nad
genima za boju kose

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

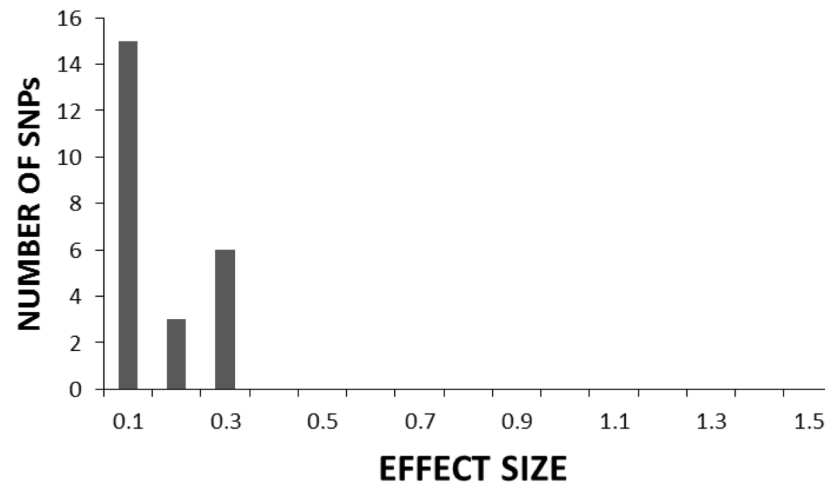
Genetska arhitektura fenotipskih svojstava

Genetska arhitektura opisuje genetske varijacije koje utječu na nasljednu fenotipsku varijabilnost

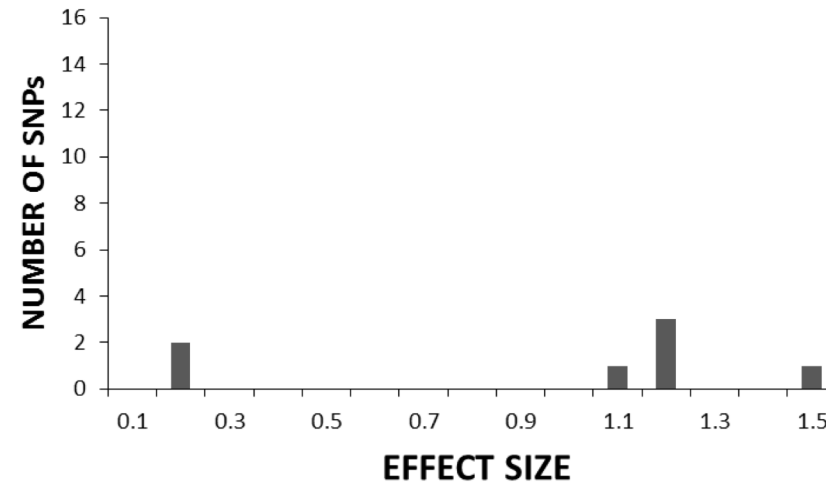
Ona ovisi o broju genetskih varijanti koje utječu na fenotipsko svojstvo, njihovu učestalost u populaciji, jačinu njihovog učinka, te njihovu međusobnu interakciju kao i interakciju sa okolišem.

Genetsku arhitekturu opisujemo kao **monogenu**, **oligogenu** i **poligenu** (jedan, nekoliko ili puno gena značajno utječu na fenotipsku varijabilnost)

Genetska arhitektura fenotipskih svojstava



POLIGENA – mnogo
lokusa malog učinka



OLIGOGENA – manji
broj lokusa, ali jačeg
učinka

Jačina učinka (x) i broj genetskih varijanti koje utječu na fenotipsko svojstvo (y)

Genetska arhitektura fenotipskih svojstava

GWAS - Genome Wide Association mapping - metoda genomske asocijacije

Kompleksnim algoritmima određuju se oni lokusi na genomu čija frekvencija alela korelira s varijabilnosti određenih fenotipskih svojstava

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

Article **Figures & Data** **Info & Metrics** **eLetters**  **PDF**

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.

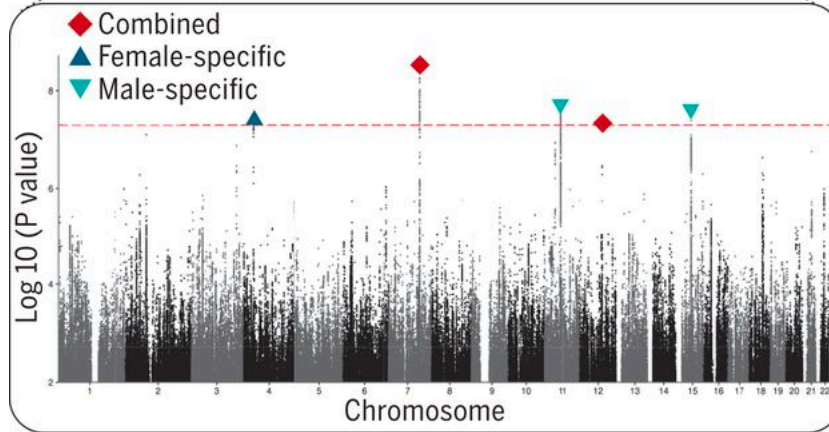
Science, this issue p. [eaat7693](#); see also p. [869](#)

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)

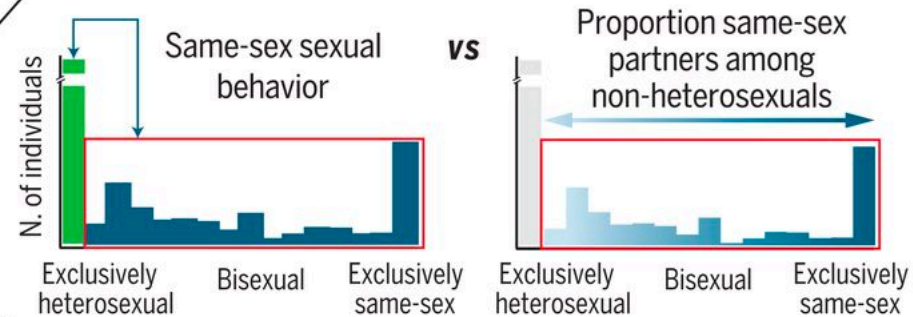
23andMe
(N=68,527)

Same-sex sexual behavior



Replication in 3
independent studies

Phenotypic complexity and heterogeneity



Genetic
architecture

Sex
differences

Biological
processes

Genetic
correlations

Communication to lay audience

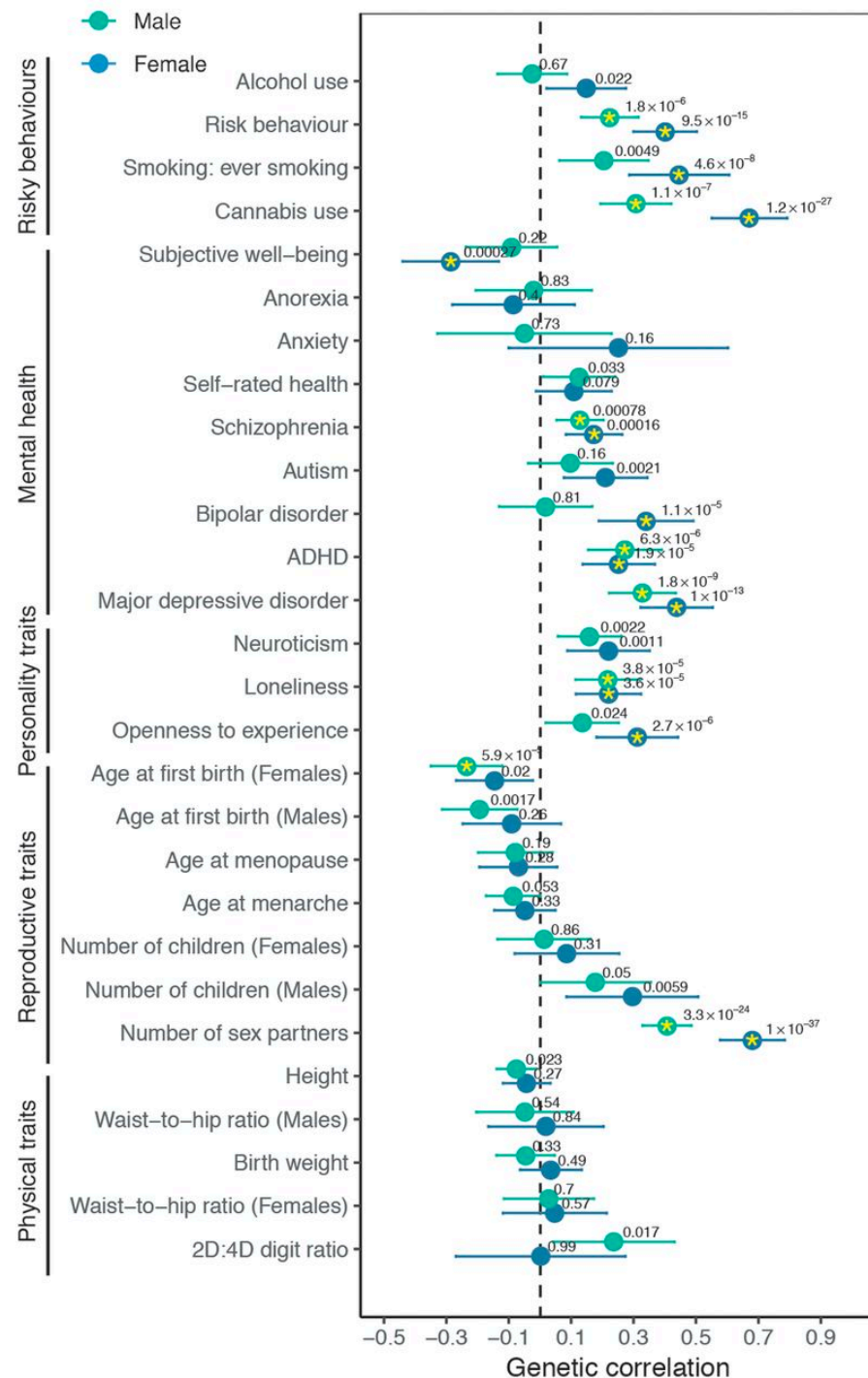


Fig. 4 Genetic correlations of same-sex sexual behavior with various preselected traits and disorders, separately for males and females. Males, green; females, blue. Yellow asterisks denote the genetic correlations that were experiment-wise significant ($P < 8.9 \times 10^{-4}$; references, definitions, 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.



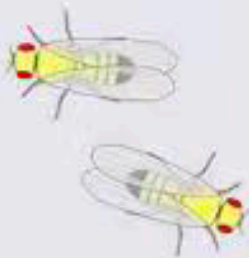
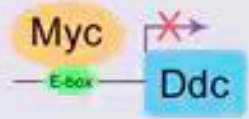
Credit: Studiotouch / Adobe Stock

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.

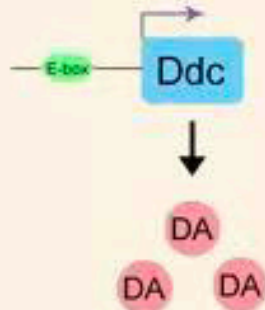
Under normal circumstances, the protein produced by the Myc gene blocks the expression of another gene called Ddc. This blocks the formation of dopamine, a neuromodulatory molecule known to facilitate courtship behavior in different species, including fruit flies and humans. Dopamine also inhibits male-male courtship in fruit flies. But when Myc is missing, dopamine is produced, and males start courting each other.

<https://doi.org/10.15252/emboj.2021109905>

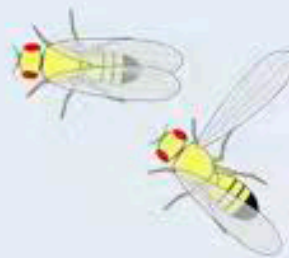
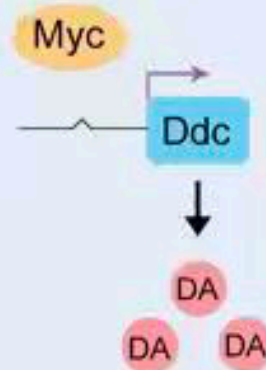
wild-type



Myc^{dm-1} mutant



Ddc^{ΔE1} mutant



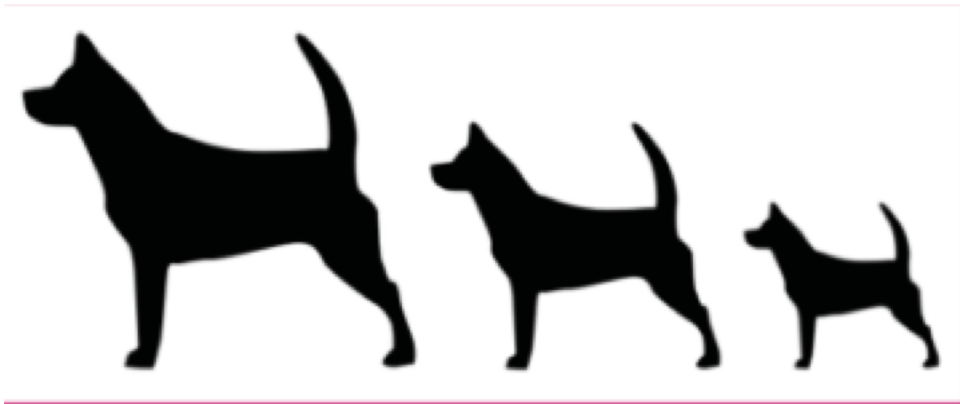
“Drosophila Myc is required in the nervous system to prevent male–male courtship in a DOPA decarboxylase (Ddc)-dependent manner, and drug-mediated Myc depletion in adult neurons suffices to elicit male–male courtship.”

- ***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.”*

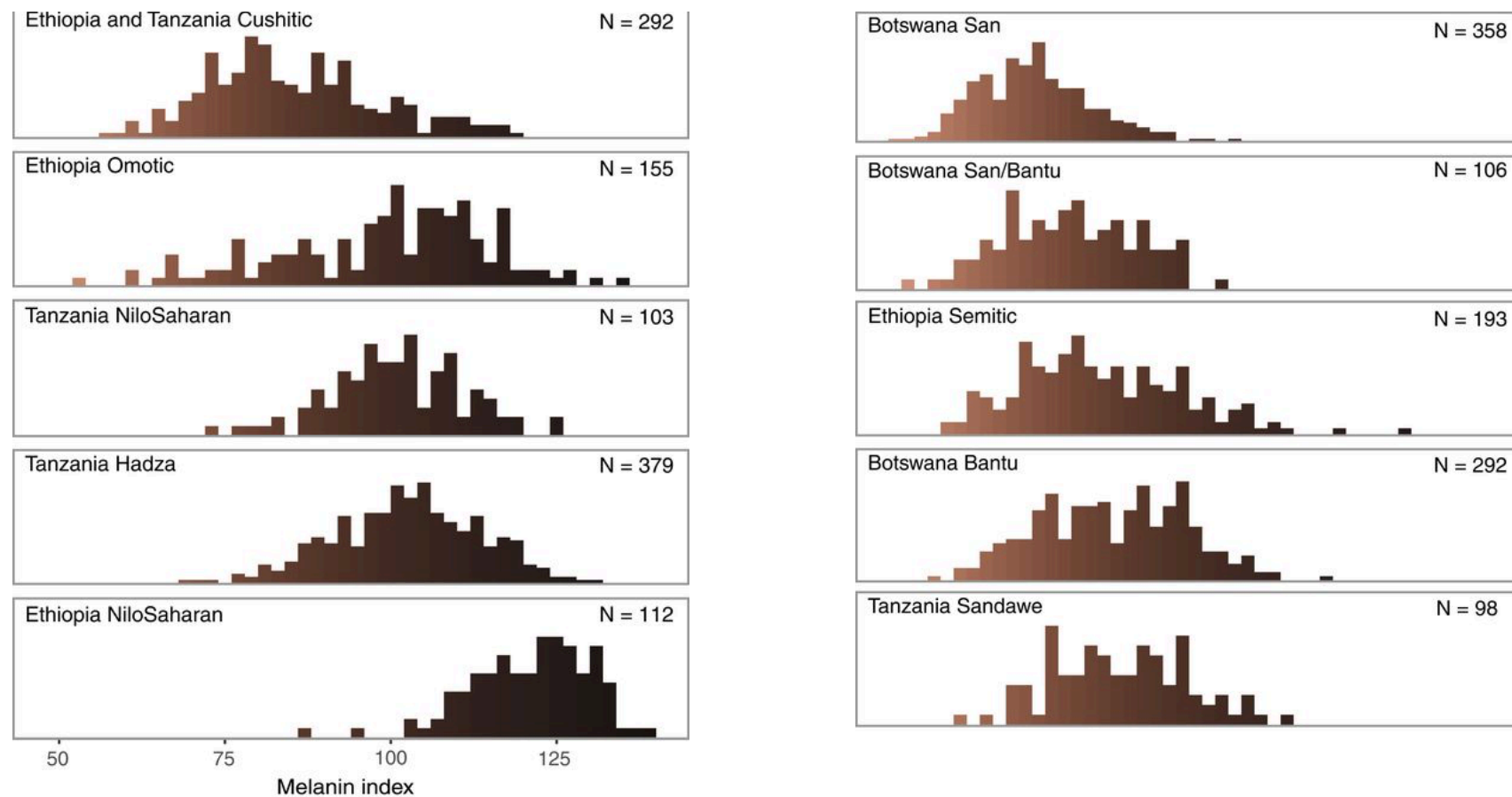
Kvantitativna svojstva

Kvantitativno svojstvo je mjerljiv fenotip koji ovisi o **kumulativnom učinku mnogih gena i okoliša**. Ta svojstva variraju u rasponu među jedinkama, i imaju **KONTINUIRANU DISTRIBUCIJU fenotipskih vrijednosti** (npr. visina, težina, krvni tlak, oblik glave)

To su **kompleksna svojstva** koja ne prate jednostavne Mendelove zakone nasljeđivanja

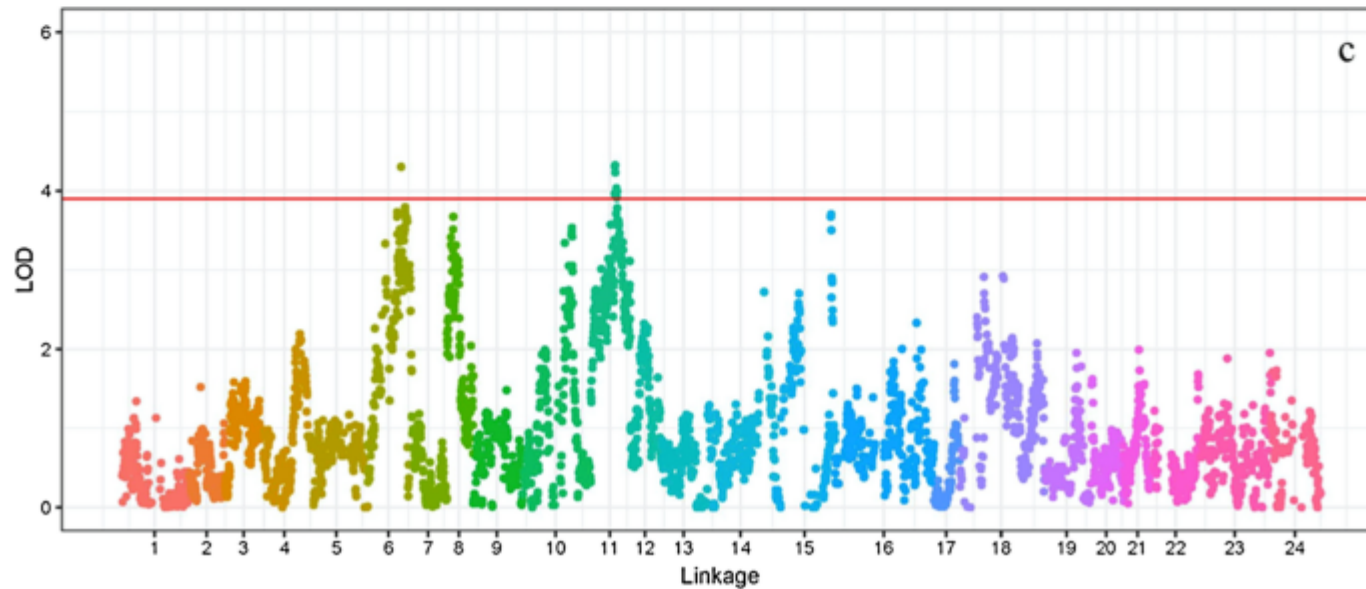


Kvantitativna svojstva – kontinuirana distribucija



Histogram indexa melanina u 10 Afričkih populacija

Kvantitativna svojstva



utjecaj pojedinih lokusa kroz 24 kromosoma na težinu jedinki ribe *Larimichthys polyactis*

QTL – *quantitative trait locus* - lokus kvantitativnog svojstva – dio kromosoma koji ima učinak na varijaciju kvantitativnog svojstva

Monogenska svojstva

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.



- Parenje se događa po mraku
- Njihovo zrikanje privlači i nepoželjne ženke: parazitske muhe, koje u njih poliježu jajašca iz kojih se liježu ličinke koje se hrane tkivom zrikavca
- Mutacija je promijenila strukturu krila mužjaka zrikavaca, od koje su izgubili sposobnost zrikanja

- jedna jedina mutacija odgovorna za ravna krila i drugačije mutacije na istom genu su se pojavile neovisno na više otoka- **KONVERGENTNA EVOLUCIJA**
- mutirani tihi mužjaci uglavnom su se držali u blizini zrikajućih mužjaka i presretali ženke koje su im dolazile
- Izravna selekcija na otoku Kauai povećala je njihovu mobilnost, da bi što lakše našli ženku
- <https://www.nature.com/news/evolution-sparks-silence-of-the-cricket-1.15323>