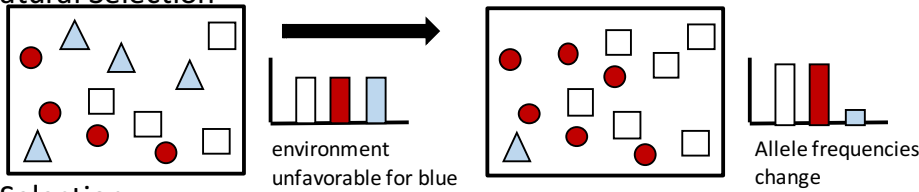
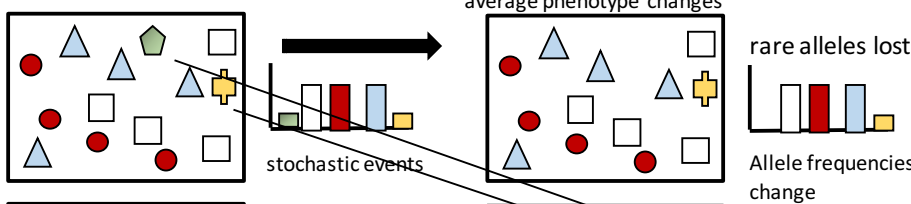


### Evolution by Natural Selection

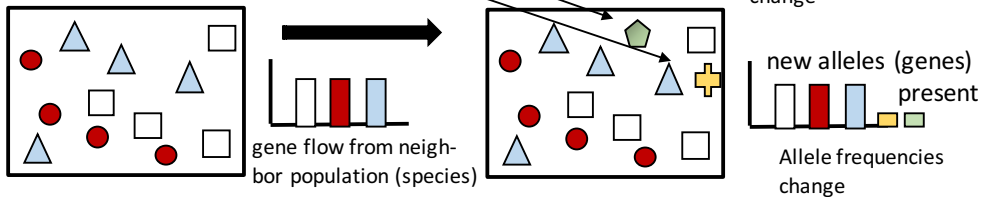


### Evolution w/o Selection

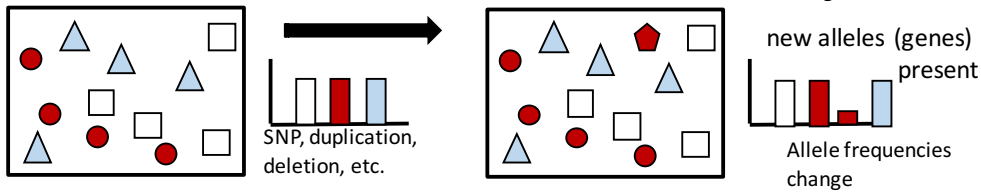
#### Drift



#### Migration (gene flow)

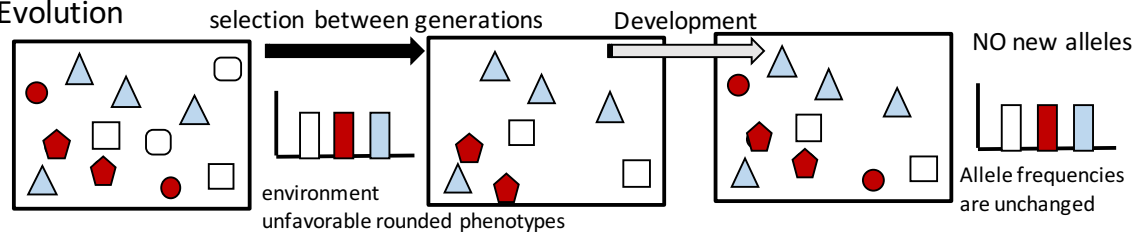


#### Mutation



### Selection w/o Evolution

#### Plasticity

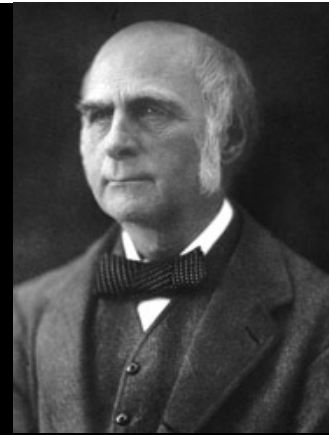


$$V_p = V_g + V_e$$

- Some phenotypic variants are favored by selection, they survive and reproduce better
- But there is no genetic basis to this variation, the individuals with greater fitness have good luck rather than good genes



GOAL: understand the genetic underpinnings of Behavior



Genes that are necessary for:  
**Single Gene**

Genes that Contribute to:  
**Quantitative or many genes**

Historic figure

Galton

Mendel  
identify dominant & recessive  
identify single genes  
define mechanisms

define Genomic Architecture  
(#, location, interaction, specificity, linkage)  
quantify variation in a population  
describe change in gene frequency

Immediate goals

Sever disruptions  
Lab induced (white coat)

Raw Materials used

Subtle variation  
Naturally occurring (rubber boot)

Tools used

Bottom Up  
Forward  
Phenotype >>> Gene  
mutagenesis/screening  
transgenesis

Top Down (= Forward)  
Observational  
Comparative Genomics  
Association mapping (GWAS)  
Experimental  
artificial selection  
crossing (artificial or natural population)  
QTL mapping  
Recombinant inbred lines  
Association Studies

Reverse  
Gene >>> Phenotype  
Knockout  
RNAi

Type of Result

Essential genes of behavior  
(newer techniques are more subtle)

Genes that Contribute to Behavior  
Factors, epistasis, GXE, probability

What observations or experiments can be used to partition phenotypic variance into its genetic and environmental components?

$$V_p = V_g + V_e$$

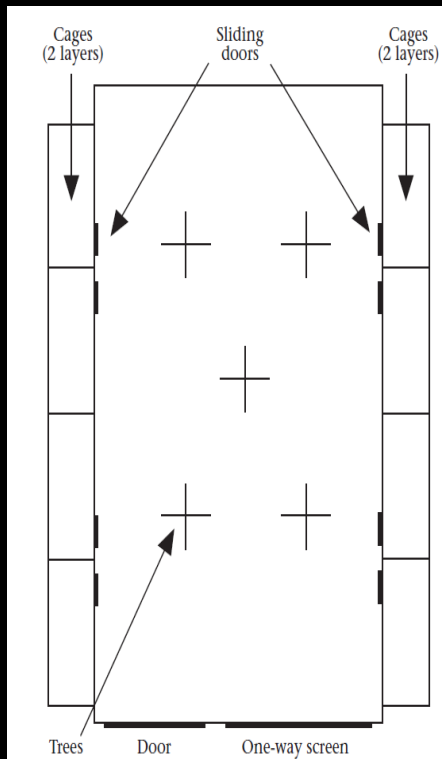
$$\text{Variance} = \frac{1}{N} \sum_{i=1}^N x_i^2 - \bar{x}^2$$

Heritability: the proportion of the phenotypic variance that is due to genetic variance

$$h^2 = V_g / V_p$$

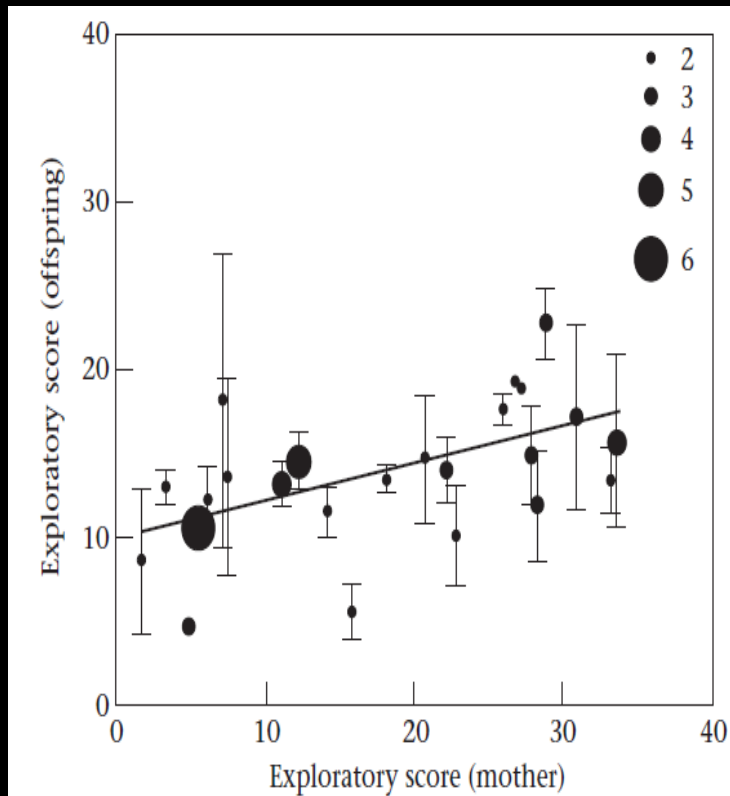
$$Variance = \frac{1}{N} \sum_{i=1}^N x_i^2 - \bar{x}^2$$

a measure of dispersion from the mean



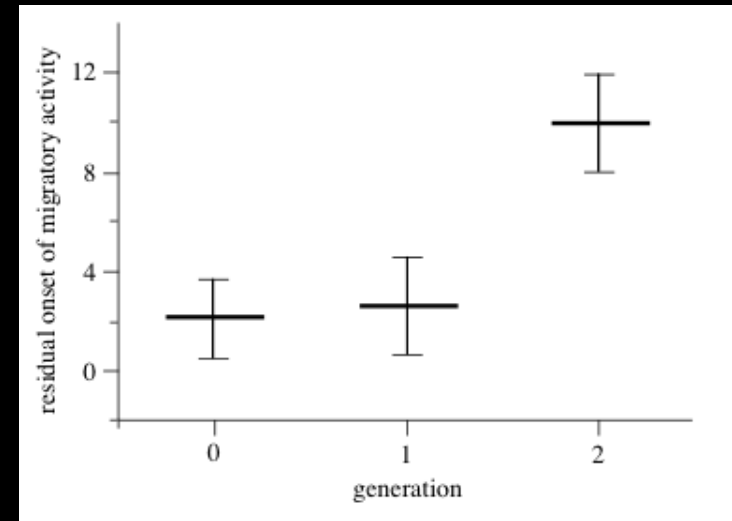
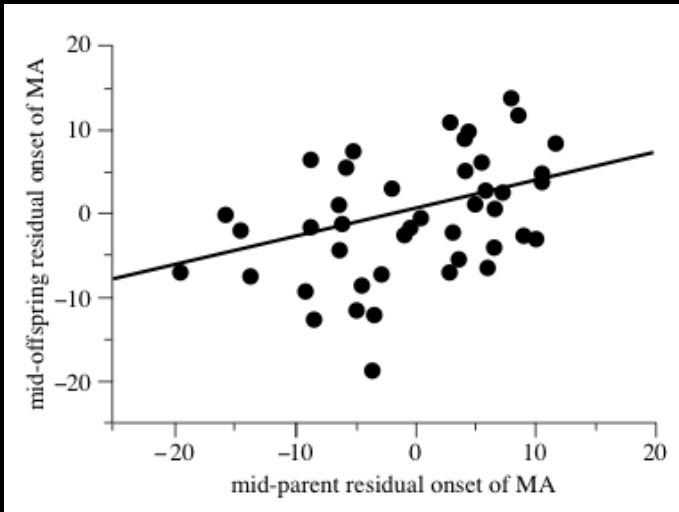
- noted where a bird was at each second in time
- noted flights and hops between locations.
- total number of flights and hops within the first 2 min = 'exploratory score'

# Heritability, Exploratory Behavior, Great Tits



- $h^2$  parent offspring regressions were 0.22-0.41
- $h^2$  sibling analyses 0.37-0.40

estimate heritability as the slope of parent/offspring correlation



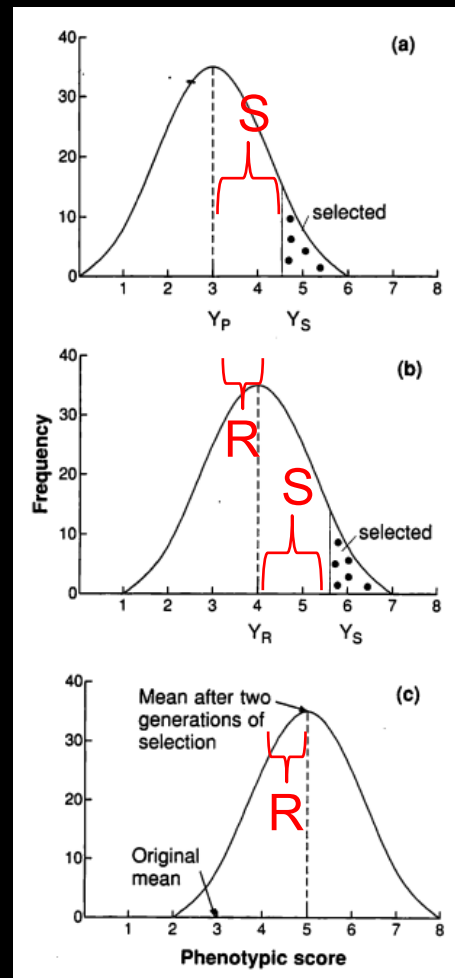
estimate heritability as the slope of parent/offspring correlation

migration timing is heritable & selectable

Pulido et al (2001) PRS 268:953-959.



# Heritability:



Note: the value for Heritability changes as The genetic variance in the Population changes

estimate heritability as response to selection divided by the strength of selection

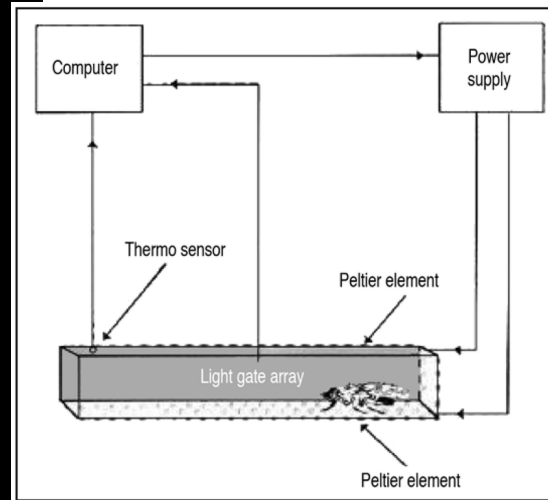
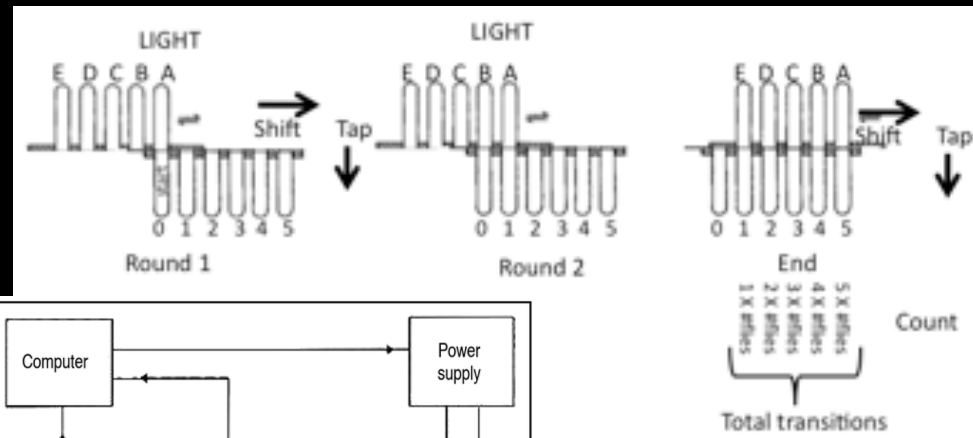
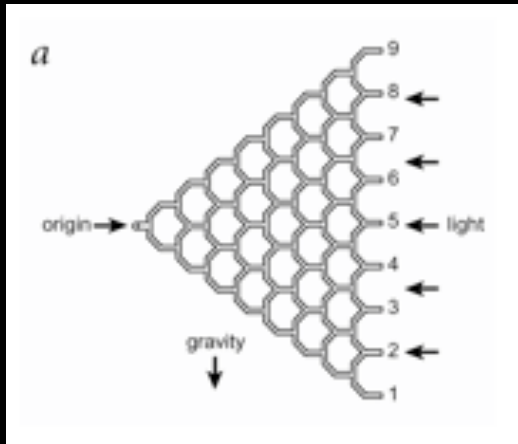
$$h^2 = R/s$$



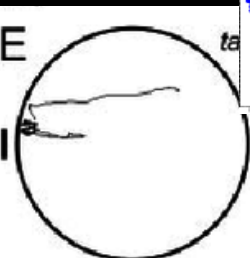
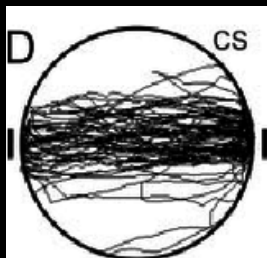
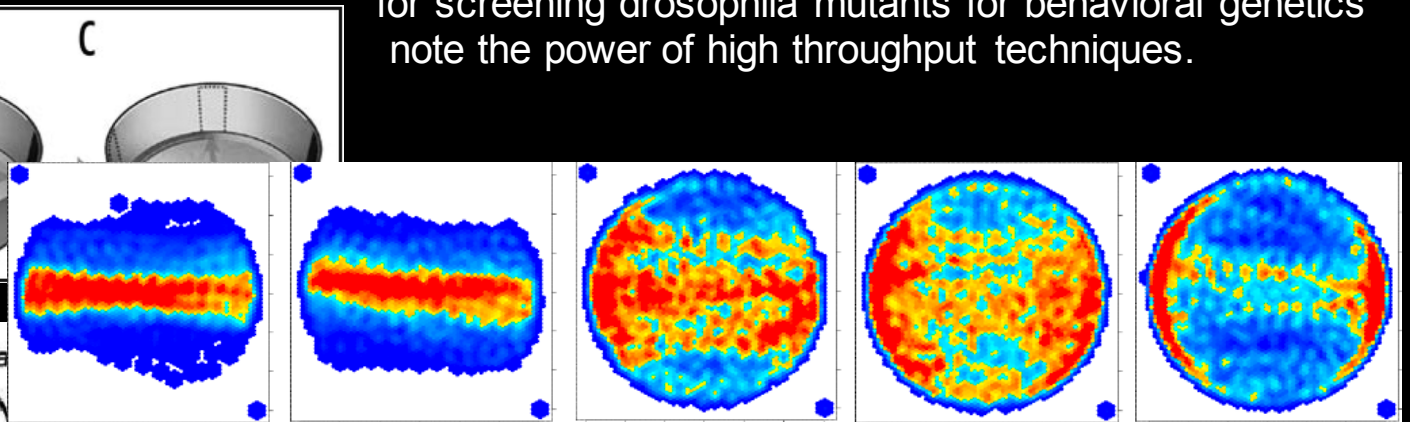
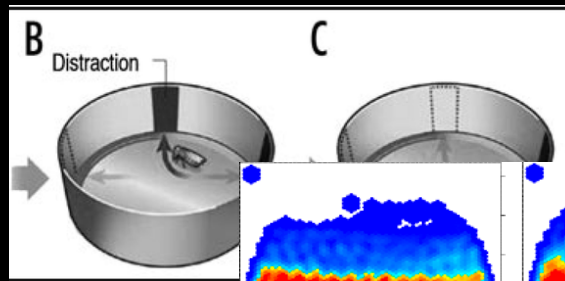
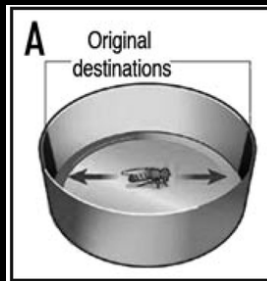
Genotype	aabb	Aabb	AAbb	AABb	AABB	AaBb	aaBb
$V_A$ 1. Additive effect Phenotypic score	0	1	2	3	4		
$V_D$ 2. Dominance effect Phenotypic score	0	2	2	4	4		
$V_I$ 3. Dominance plus epistatic effect Phenotypic score	0	0	0	4	4		

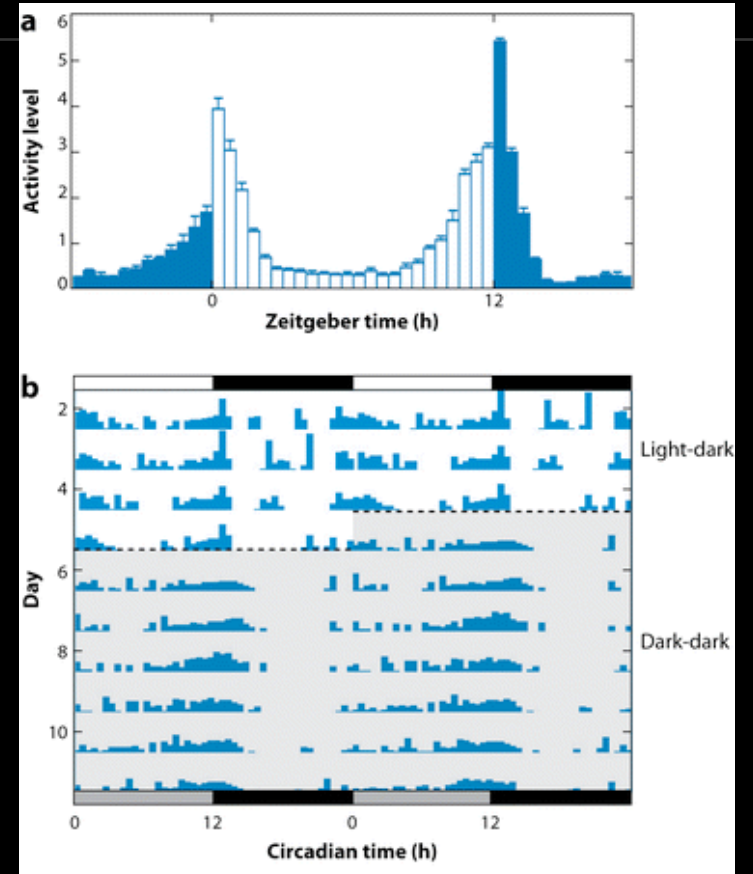
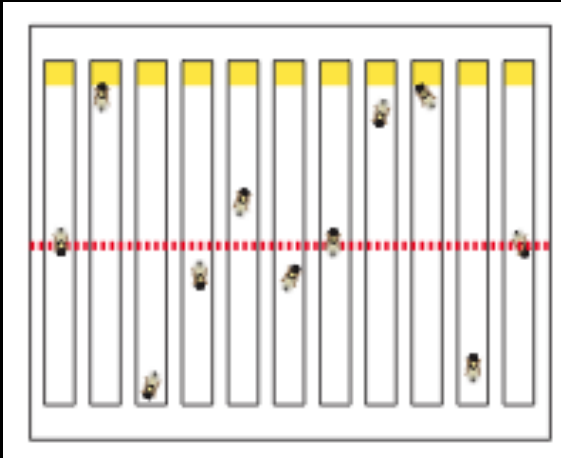
estimate heritability generally capture the additive genetic variation

## Components of Genetic Variance ( $V_g$ )

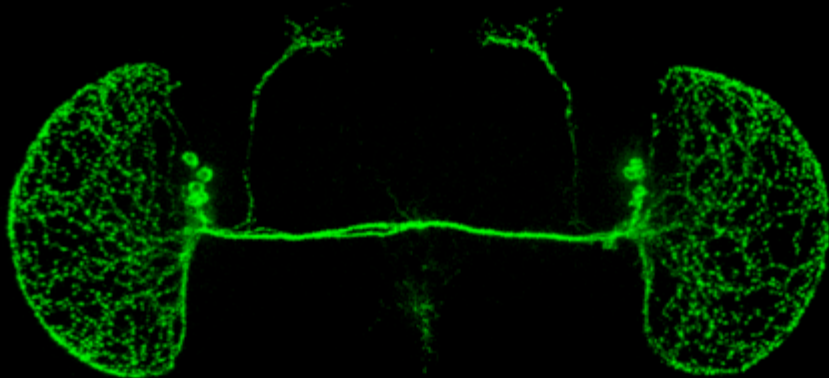
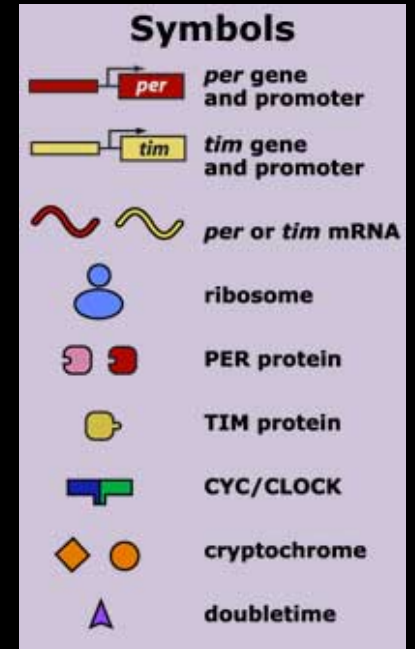
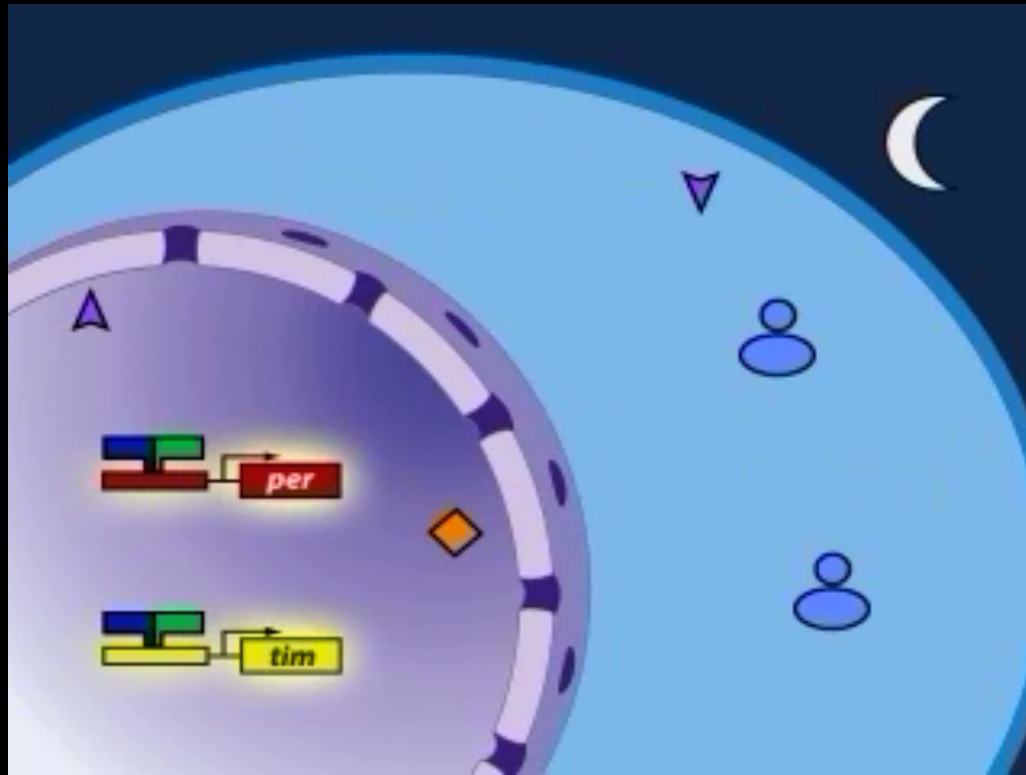


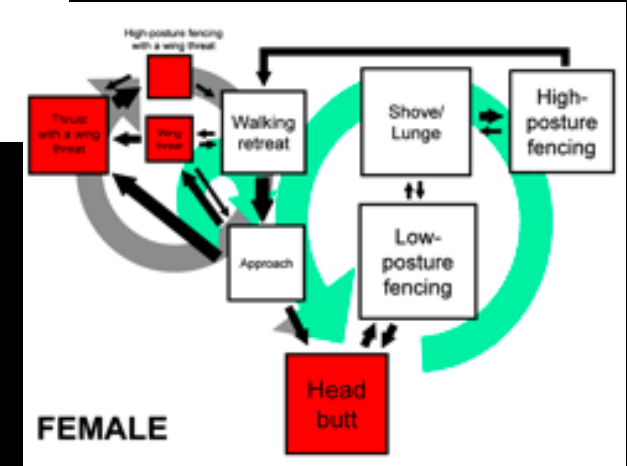
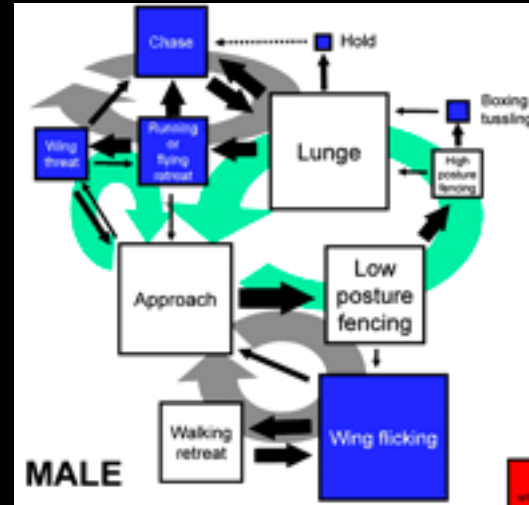
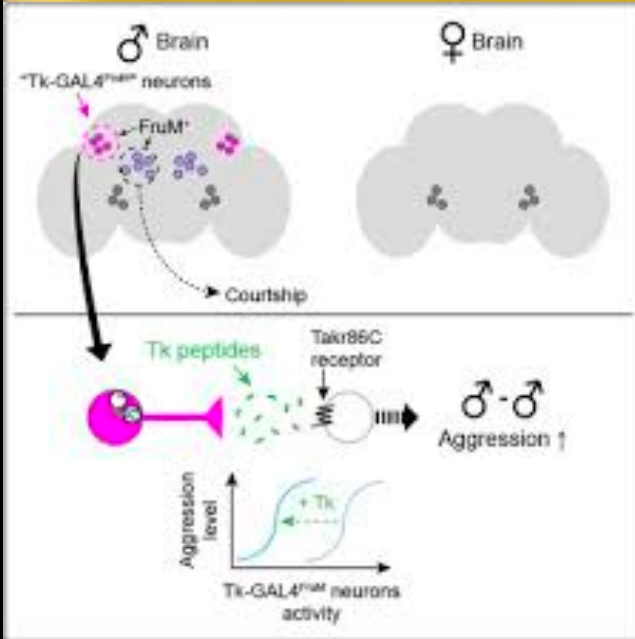
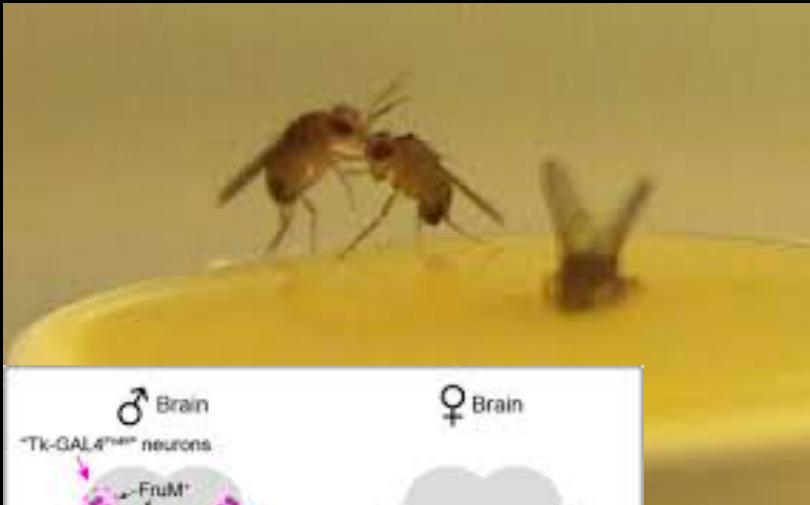
examples of classical and modern behavioral assays used for screening drosophila mutants for behavioral genetics note the power of high throughput techniques.



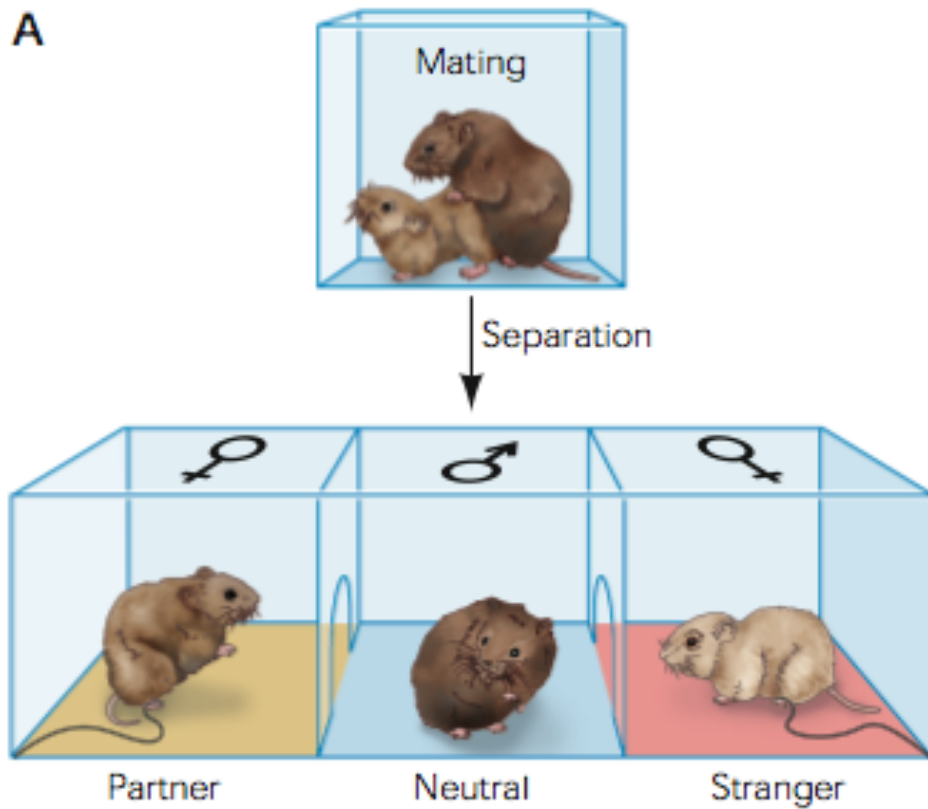
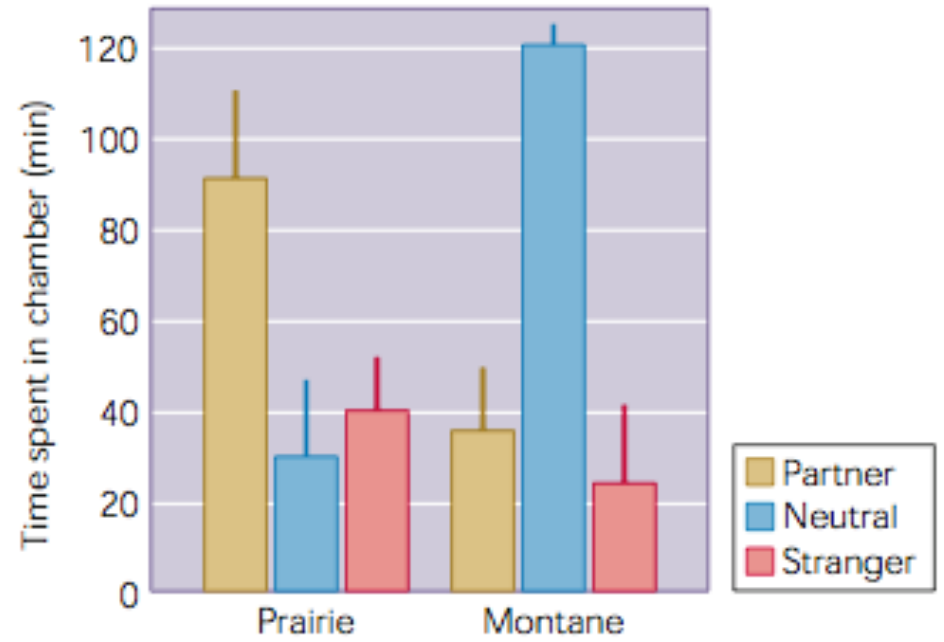


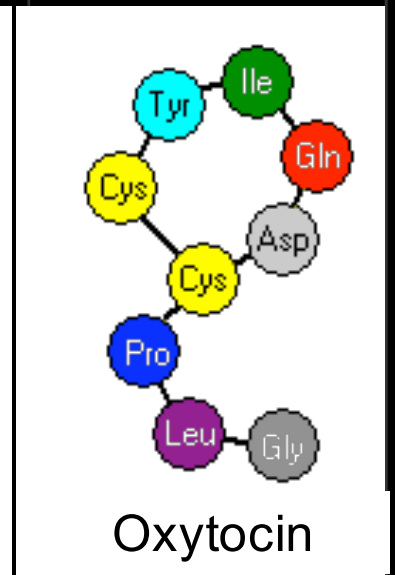
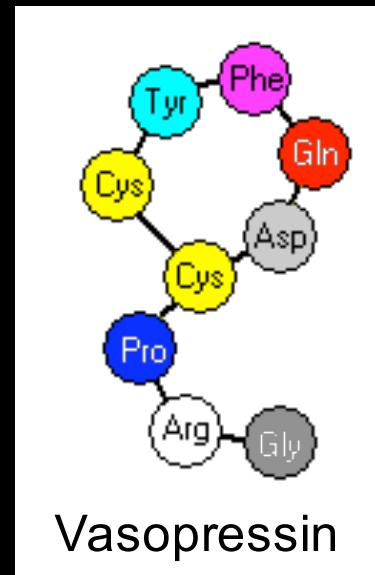
Seymour Benzer: single gene





Not all drosophila assays are high throughput

**A****B**

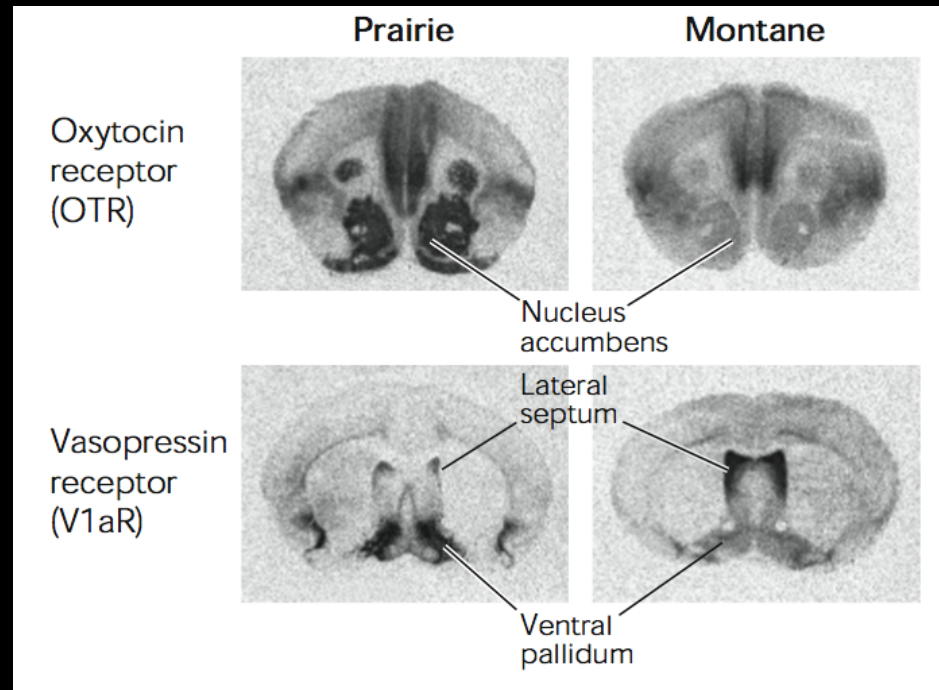


injection of AVP  
facilitates pair bond  
formation in male  
monogamous voles

injection of OT  
facilitates pair bond  
formation in female  
monogamous voles

## Monogamous

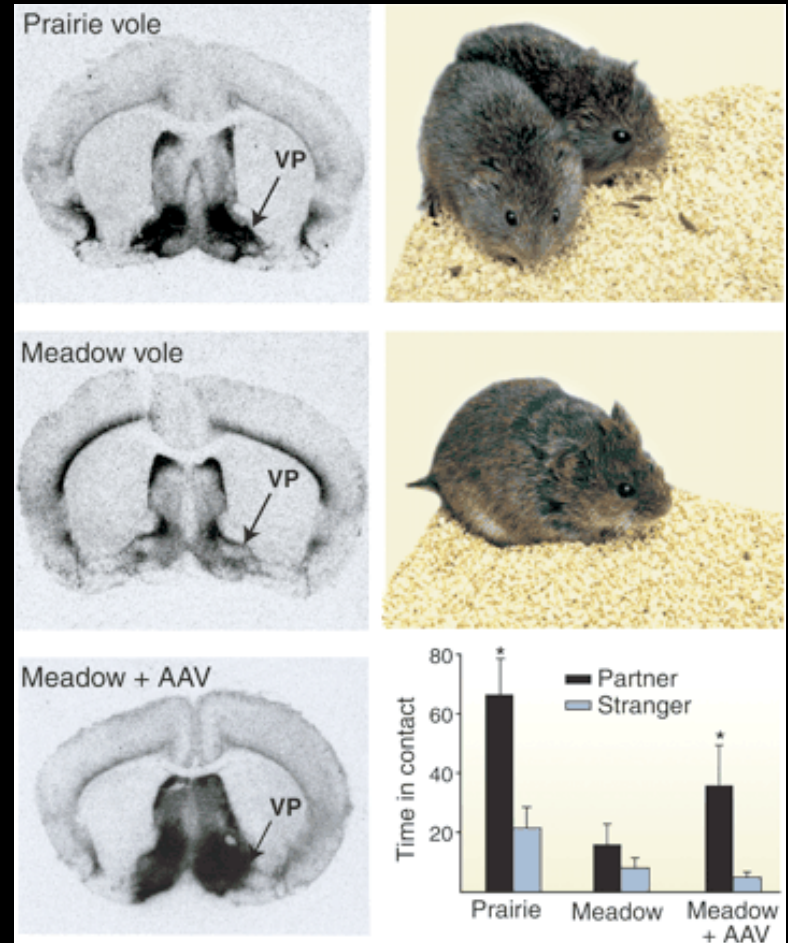
## Promiscuous





# Autoradiography

Viral vector to increase V1aR



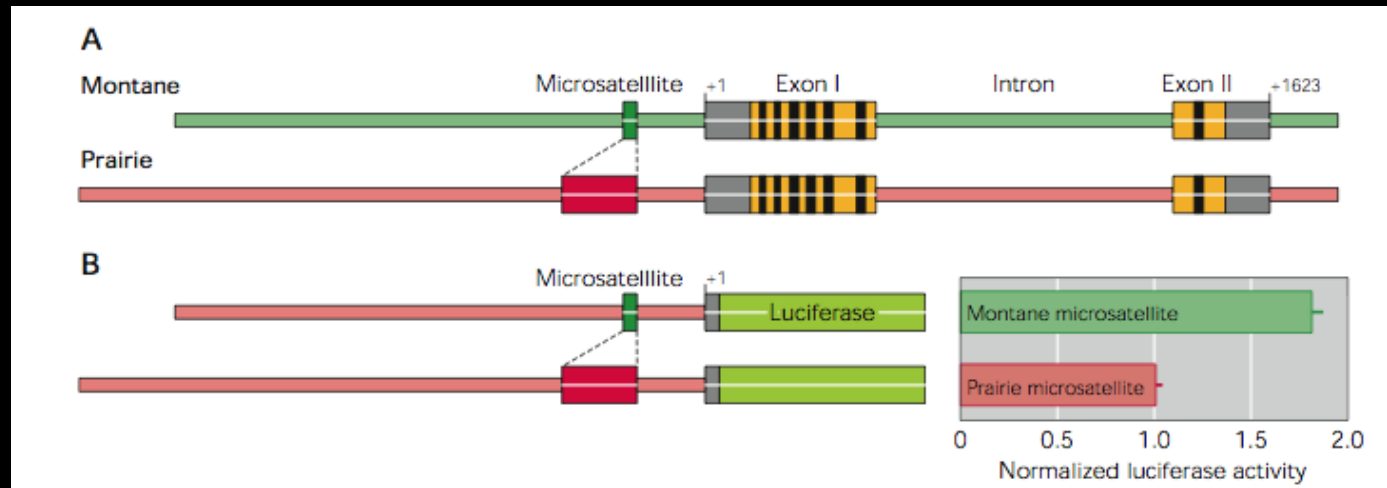
Nature 429, 754-757 (17 June 2004) | doi:10.1038/nature02539; Received 29 January 2004; Accepted 2 April 2004

Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene

Miranda M. Lim<sup>1</sup>, Zuoxin Wang<sup>2</sup>, Daniel E. Olazábal<sup>1</sup>, Xianghui Ren<sup>3</sup>, Ernest F. Terwilliger<sup>3</sup> & Larry J. Young<sup>1</sup>

Promiscuous

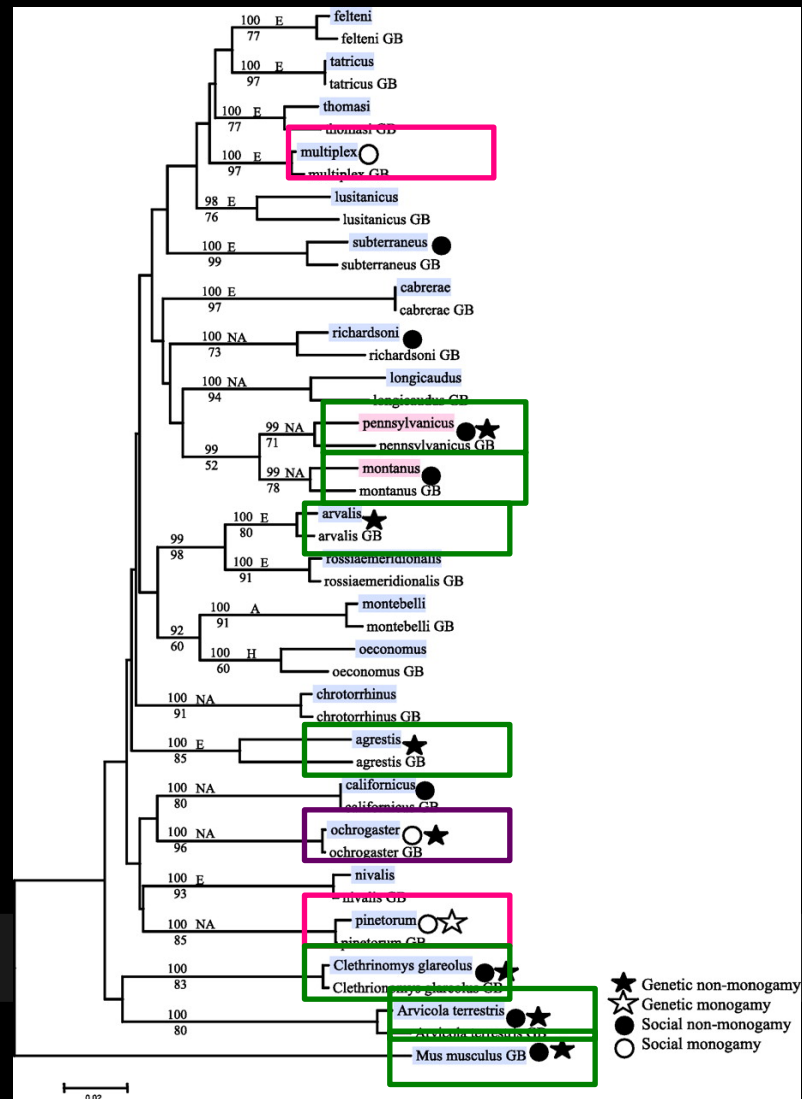
Monogamous



# Behavior

Promiscuous

Monogamous



# Behavior

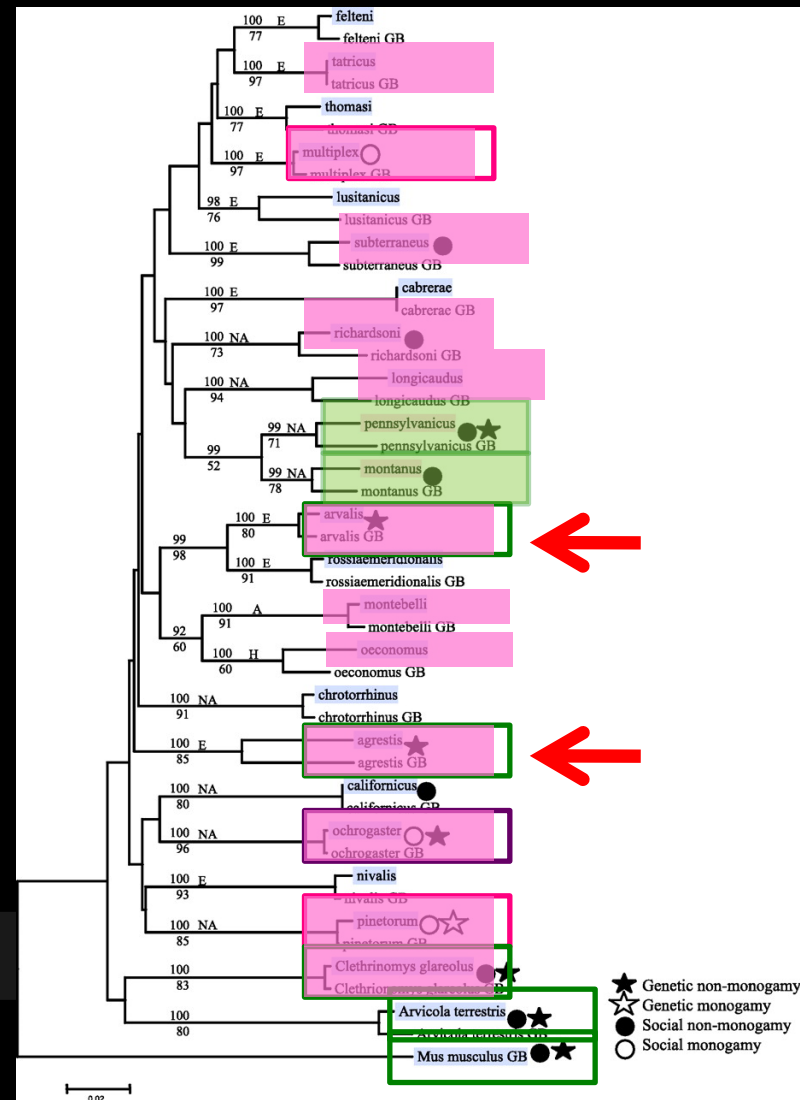
Promiscuous

Monogamous

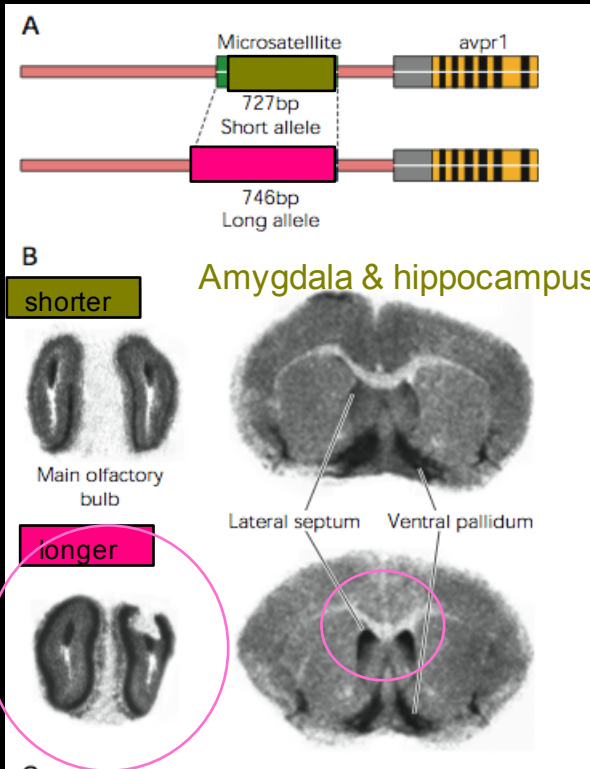
# Genetic Marker

Promiscuous

Monogamous



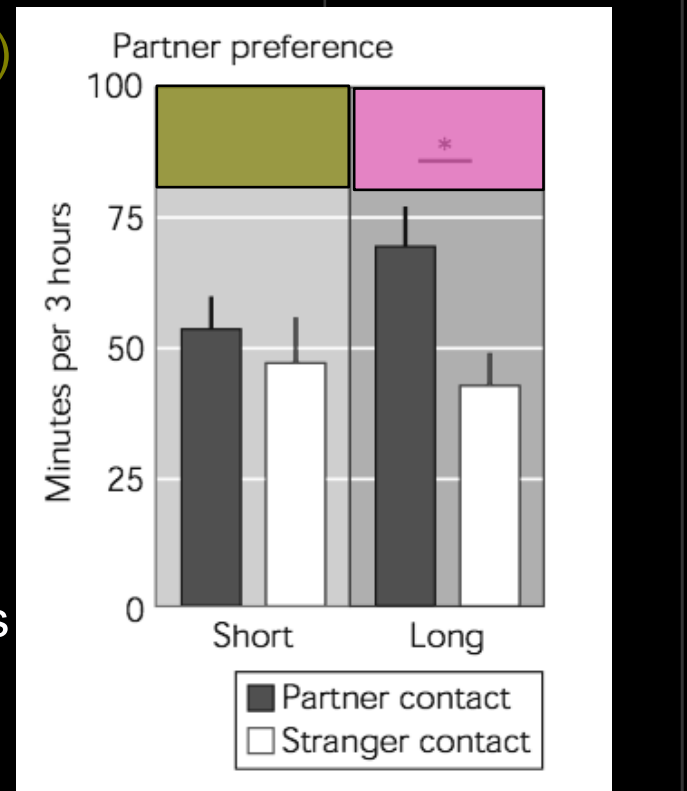
note mismatch of genotypes and phenotype called into question the causal relationship



Shorter (montane vole-like)

Longer (prairie vole-like)

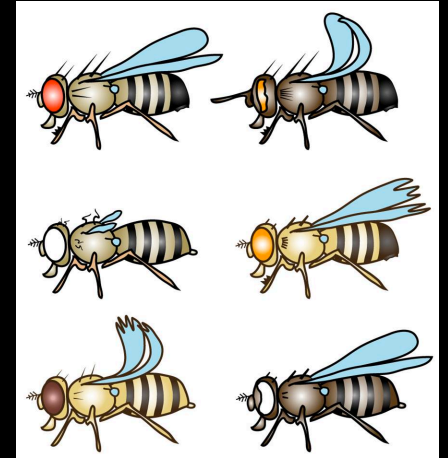
within species variation  
parallels between species

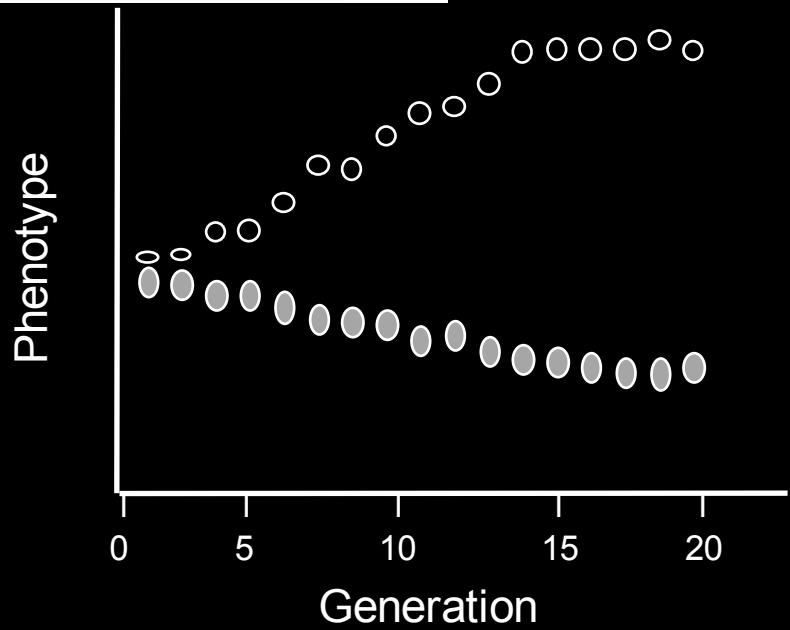
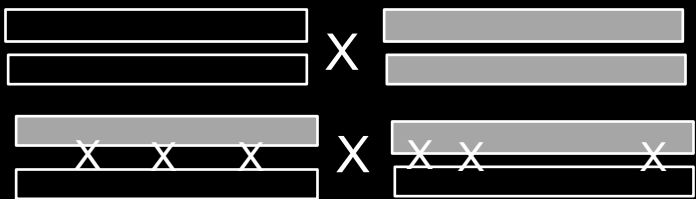
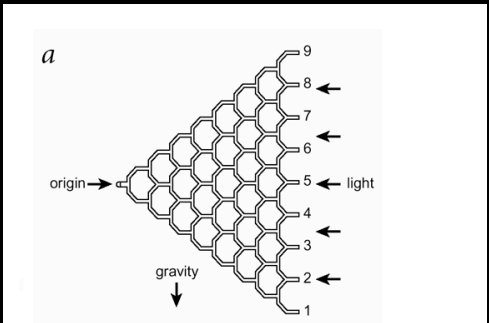


# Genetic markers

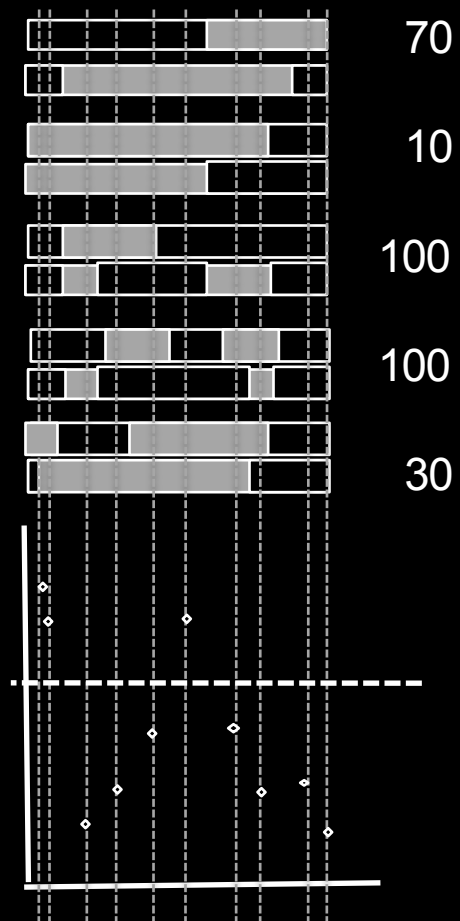
A genetic marker is an alteration in the genomic DNA (polymorphic) that can be observed (by either sequence or phenotypic result) with a known location on a chromosome.

A genetic marker can be used to identify whether an individual has certain genomic DNA at this location.



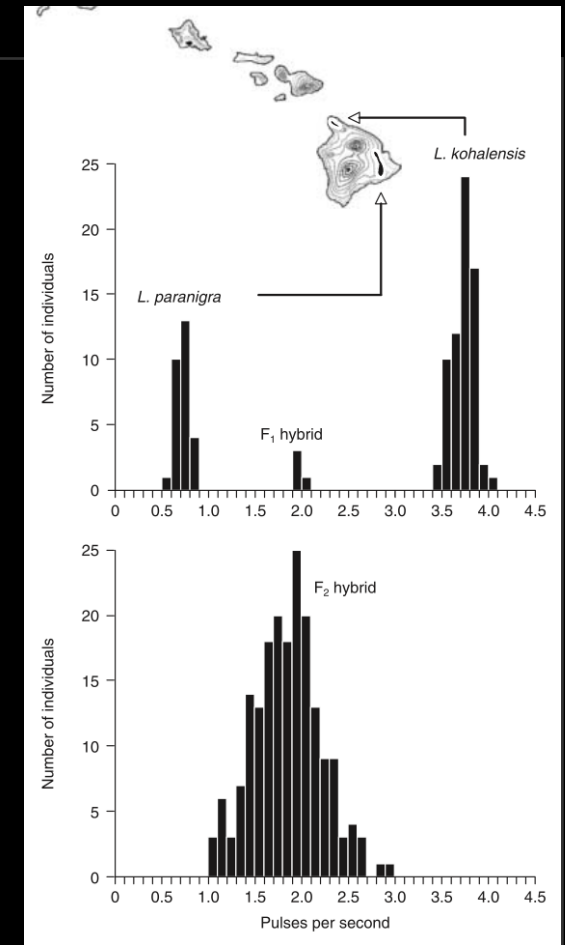
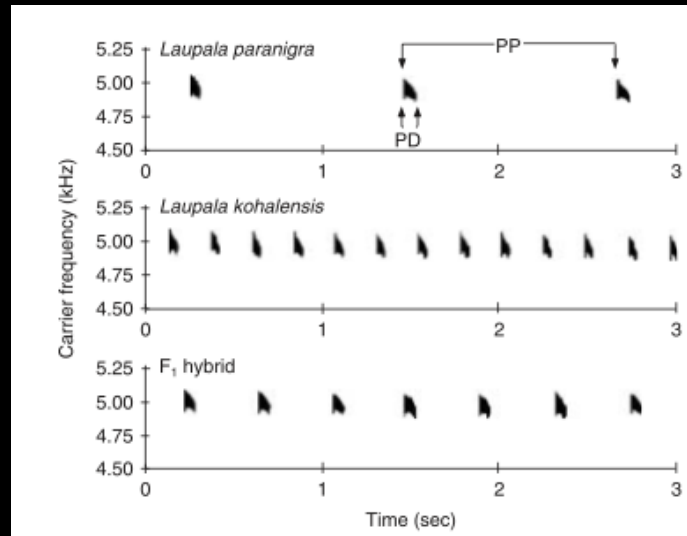


Statistical Association



Phenotype score

# Two camps QTL Studies –



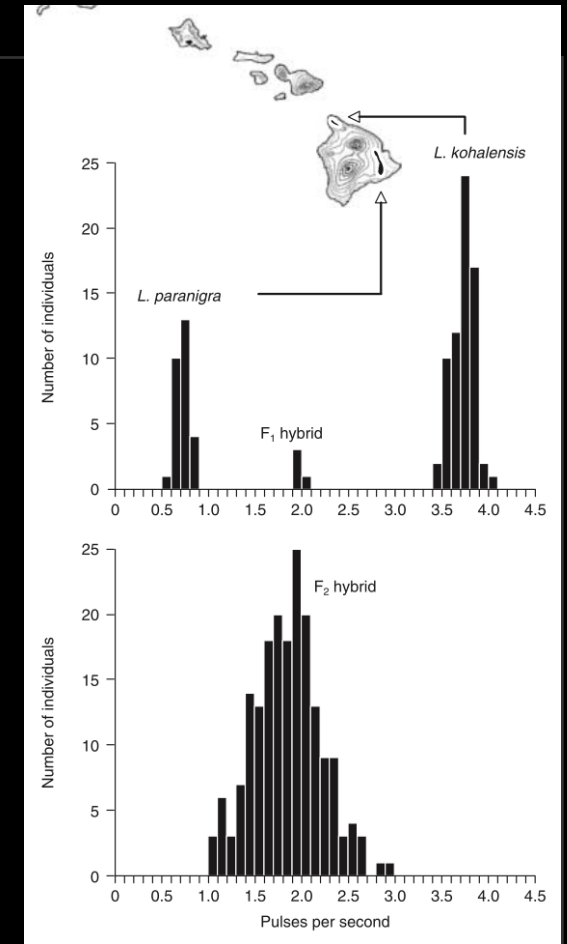
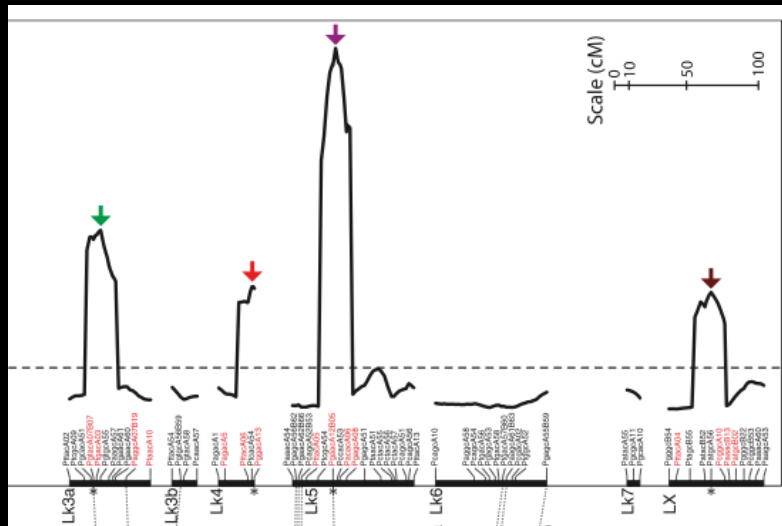
**Requirement # 1: strains with different phenotypes**

**Requirement #2 : genetic markers**

**Requirement #3 : ability to cross**



# Two camps QTL Studies – Top Down



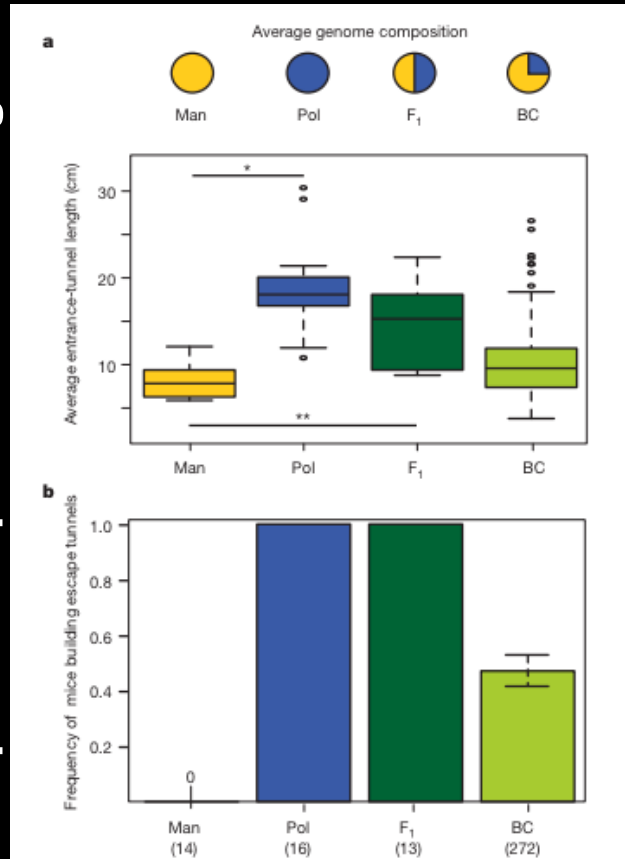
Shaw Lab



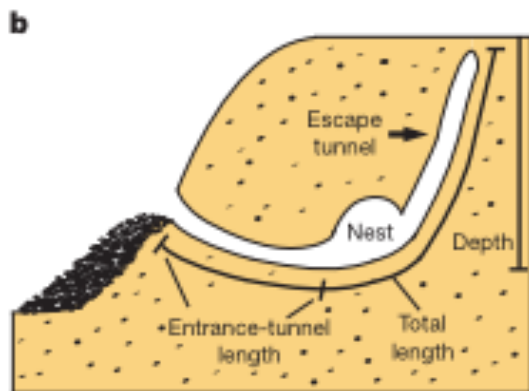
Hopi Hoekstra

tunnel length

Freq. w/ escape



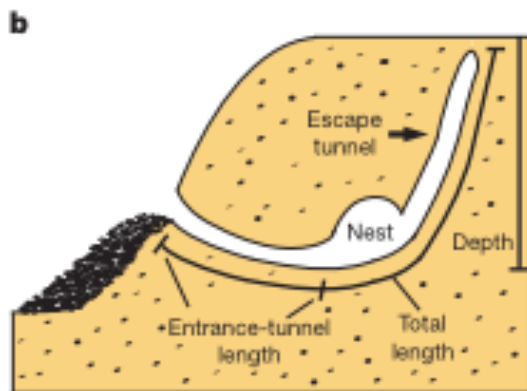
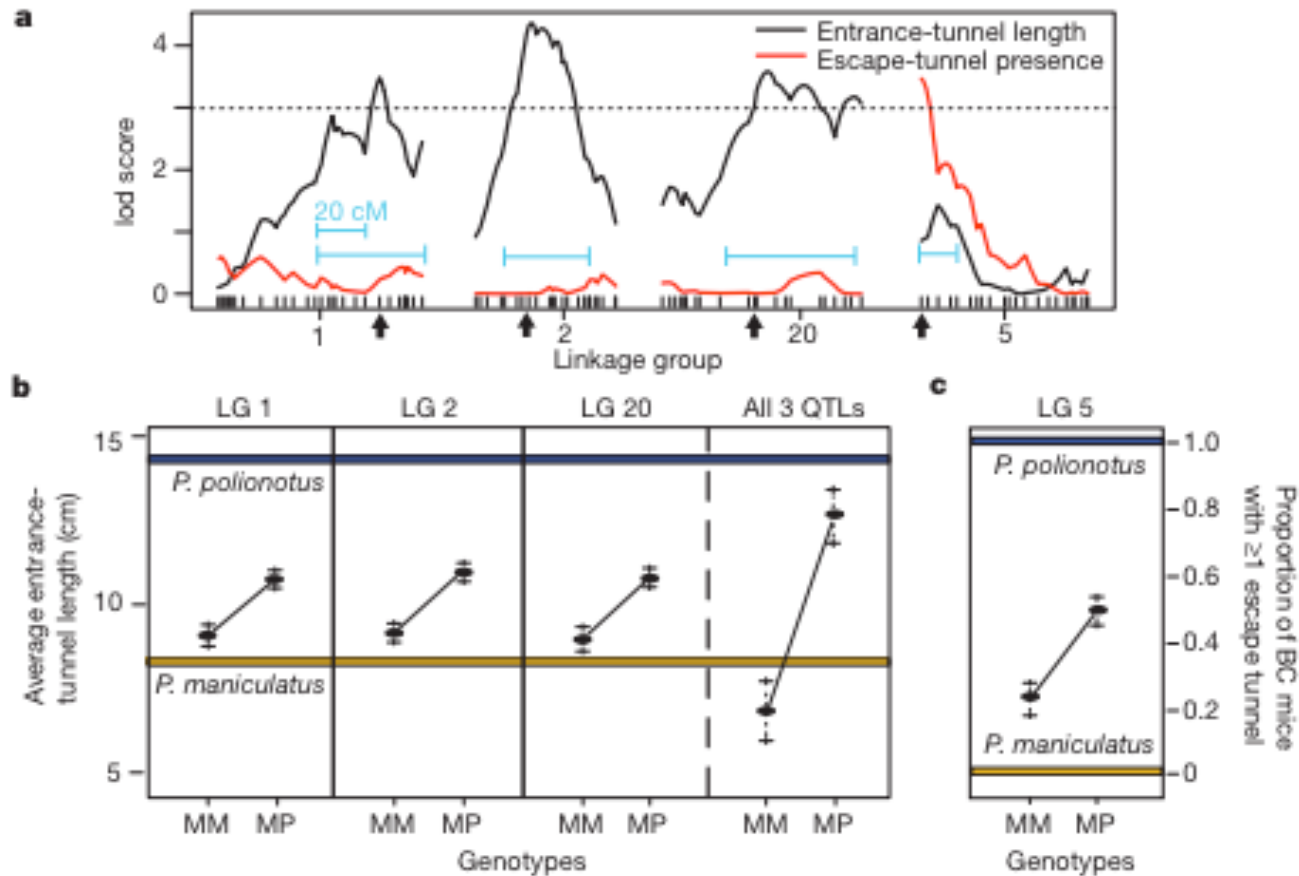
*P. maniculatus*  
*P. polionotus*



doi:10.1038/nature11816

Discrete genetic modules are responsible for complex burrow evolution in *Peromyscus* mice

Jesse N. Weber<sup>1†</sup>, Brant K. Peterson<sup>1,2</sup> & Hopi E. Hoekstra<sup>1,2</sup>



**526 loci surveyed w/ Rad-seq  
272 backcross mice assayed**





isogenic lines or recombinant inbred lines capture some of the natural genetic variation but allow you to retest stocks for which genome sequence info may be available.

## WELCOME TO THE MACKAY LABORATORY

The Genetic Basis of Quantitative Variation

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### 2015 Publications

- Arya, G. H., Magwire, M. M., Huang, W., Serrano-Negron, Y. L., Mackay, T. F. C. & Anholt, R. R. H. 2015. The genetic basis for variation in olfactory behavior in *Drosophila melanogaster*. *Chem. Senses* 40: 233-243. PMID: in progress [\[pdf\]](#)
- Gaertner, B. E., Ruedi, E. A., McCoy, L. J., Moore, J. M., Wolfner, M. F. & Mackay, T. F. C. 2015. Heritable variation in courtship patterns in *Drosophila melanogaster*. *G3* 5: 531-539. PMID: PMC4390569 [\[pdf\]](#)
- Dembeck, L. M., Huang, W., Magwire, M. M., Lawrence, F., Lyman, R. F. & Mackay, T. F. C. 2015. Genetic architecture of abdominal pigmentation in *Drosophila melanogaster*. *PLoS Genetics* *PLoS Genet* 11: e1005163 PMID: PMC4416719 [\[pdf\]](#)
- Ivanov, D. K., Escott-Price, V., Ziehm, M., Magwire, M. M., Mackay, T. F. C., Partridge, L. & Thornton, J. M. 2015. Longevity GWAS using the *Drosophila* Genetic Reference Panel. *J. Gerontol.*, in press [\[pdf\]](#)
- Morgante, F., Sørensen, P., Sorensen, D. A., Maltecca, C. & Mackay, T. F. C., 2015. Genetic architecture of micro-environmental plasticity in *Drosophila melanogaster*. *Scientific Reports* 5: 9785. PMID: PMC4421828 [\[pdf\]](#)
- Ober, U., Magwire, M. M., Huang, W., Schlather, M., Simianer, H. & Mackay, 2015. Accounting for genetic architecture improves sequence based genomic prediction for a *Drosophila* fitness trait. *PLoS One* 10: e0126880. PMID: PMC4423967 [\[pdf\]](#)
- Shorter, J. R., Couch, C. R., Huang, W., Carbone, M. A., Peiffer, J., Anholt, R. R. H. & Mackay, T. F. C. 2015. Epistasis and the genetic architecture of *Drosophila* aggressive behavior. *PNAS*, in press [\[pdf\]](#)

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