Deleterious Selective Sweeps

Floyd A. Reed
MPI Evolutionary Biology

Hitchhiking mapping: A population-based fine-mapping strategy for adaptive mutations in *Drosophila melanogaster*

Bettina Harr*, Max Kauer, and Christian Schlötterer†

PNAS | October 1, 2002 | vol. 99 | no. 20 | 12949–12954

An Improved Method for Estimating the Rate of Fixation of Favorable Mutations Based on DNA Polymorphism Data

Wolfgang Stephan
Department of Zoology, University of Maryland

Mol. Biol. Evol. 12(5):959–962. 1995.

Adaptive hitchhiking effects on genome variability

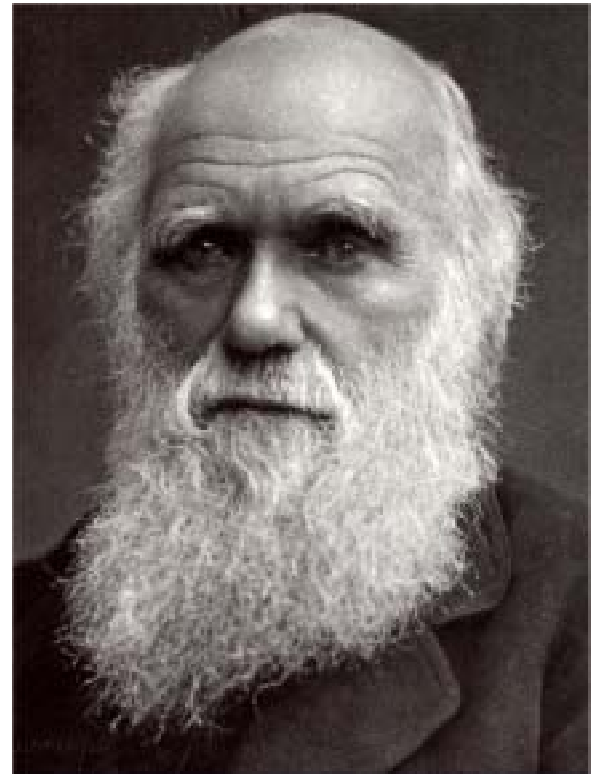
Peter Andolfatto

Current Opinion in Genetics & Development 2001, 11:635–641

Darwin:

-Natural variation exists and is heritable.
-More organisms are born than can survive.
-Therefore, **organisms best suited to the environment** survive more often and slight differences may accumulate over time.

Gradual evolution of a species by natural selection!

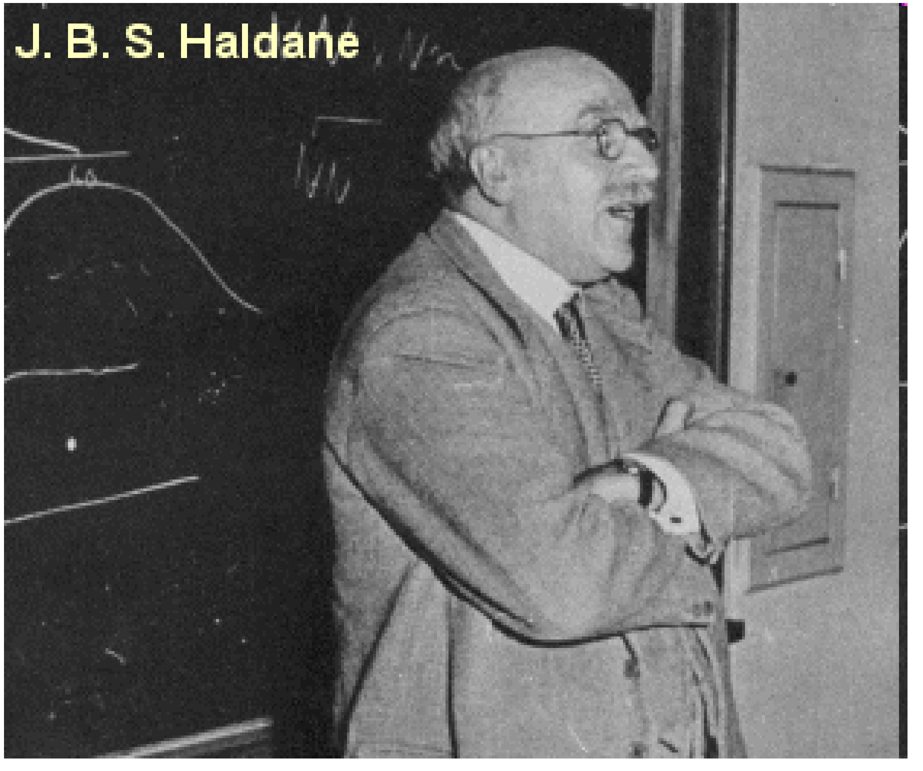


Huxley:

"How extremely stupid not to have thought of that!"

Haldane:

"Clearly, a higher plant species is at the mercy of its pollen grains."



In addition to underdominance, we are very interested in genetic systems that can "drive" alleles into populations.

These systems not only have the capacity to transform wild populations, but can be important evolutionary forces.

“Non-adaptive” systems that can result in or mimic selective sweeps

Meiotic Drive
Parrondo’s Paradox *
Underdominance
Background-selection
Hotspots of recombination

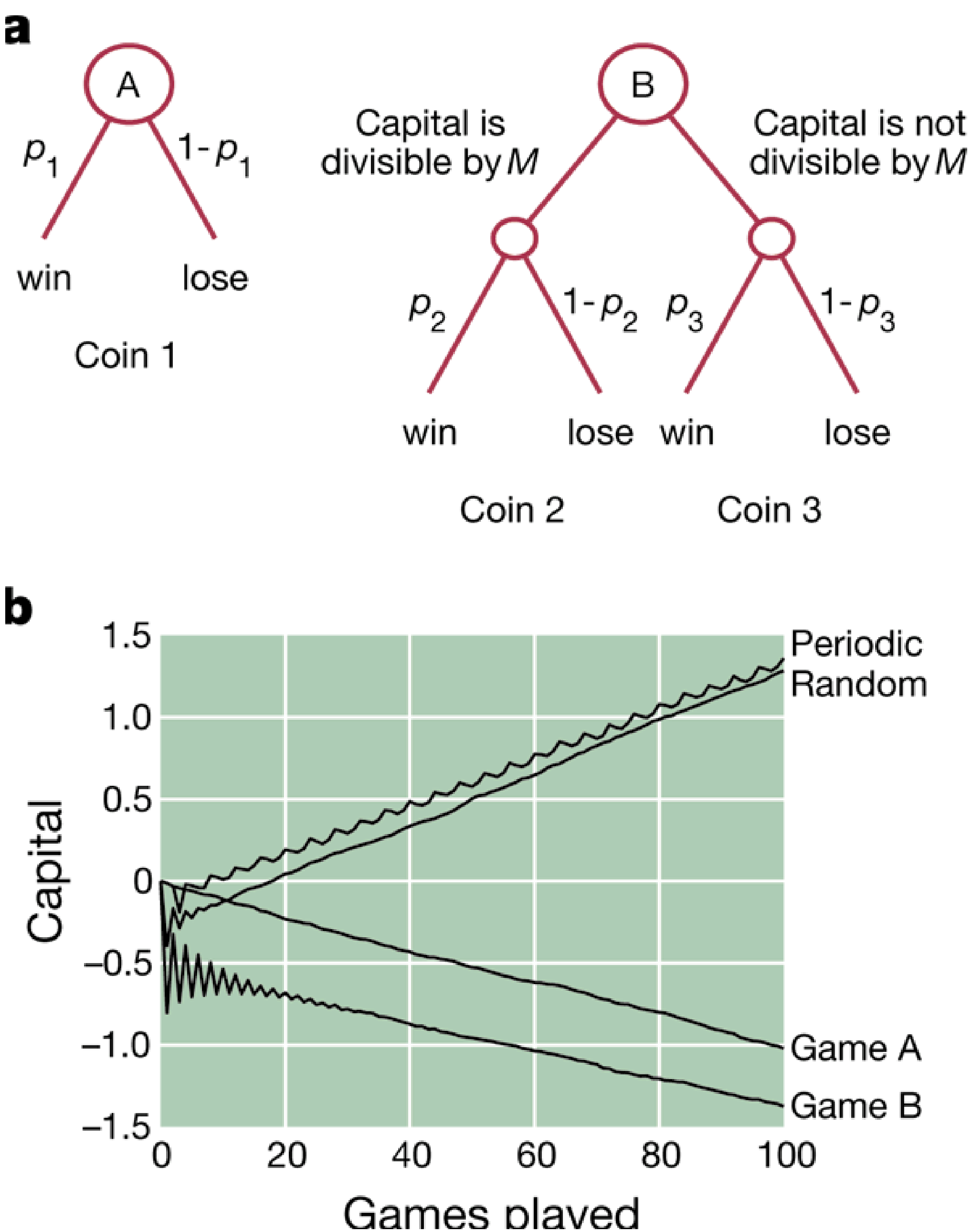
What is Parrondo’s Paradox?

What is Parrondo’s Paradox?

“A losing strategy that wins”

“Given two games, each with a higher probability of losing than winning, it is possible to construct a winning strategy by playing the games alternately.“

http://en.wikipedia.org/wiki/Parrondo%27s_paradox



Two games with losing expectations.

One is a simple win/lose with a slightly higher chance of losing ($p_1<1/2$).

The other consists of subgames with a rule to use to pick which subgame (M=3).

One subgame has a winning expectation ($p_3=3/4$), which is outweighed by a losing expectation ($p_2=1/10$).

(Harmer and Abbott 1999)

Excitement

Excitement and Controversy

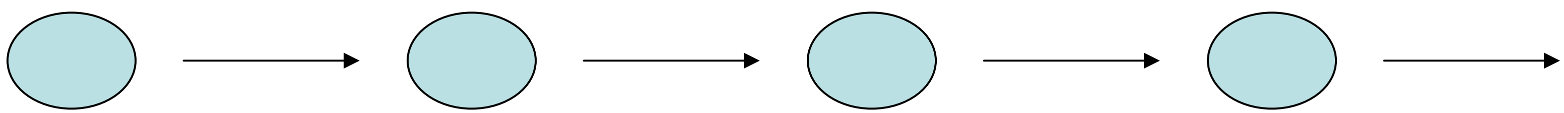
Iyengar, R., and R. Kohli, 2004 Why Parrondo's paradox is irrelevant for utility theory, stock buying, and the emergence of life: Can losses be combined to give gains? *Complexity* 9: 23–27.

A key compoenent of Parrondian systems is that one of the games must be a second-order (or higher) Markov-chain process (Iyengar and Kohli 2004).

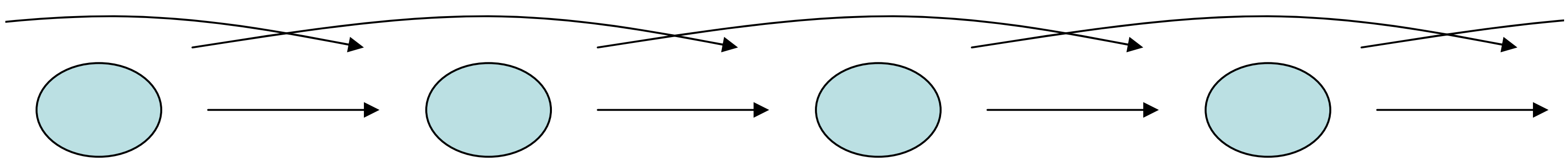
The next state is dependant on at least two current or previous states.

The capital, and thus the chance of winning or losing, depends on multiple previous wins/loses.

First Order



Second Order



Could Parrondo's Paradox work in a population genetic system?

The Genetic System

Chromosome	Gene	Allele	Frequency
X-chromosome	Ξ	ξ	x
Autosome	Δ	δ	a

The Genetic System

Chromosome	Gene	Allele	Frequency
X-chromosome	Ξ	ξ	x
Autosome	Δ	δ	a

$$\xi \xrightarrow{\text{Transactivator}} \delta$$

The Genetic System

Chromosome	Gene	Allele	Frequency
X-chromosome	Ξ	ξ	x
Autosome	Δ	δ	a

Gene product results in sexually antagonistic selection

Transactivator

$$\xi \xrightarrow{\text{Transactivator}} \delta \nearrow$$

The Genetic System

Chromosome	Gene	Allele	Frequency
X-chromosome	Ξ	ξ	x
Autosome	Δ	δ	a

$$\xi \xrightarrow{\text{Transactivator}} \delta \rightarrow \text{Gene product results in sexually antagonistic selection}$$

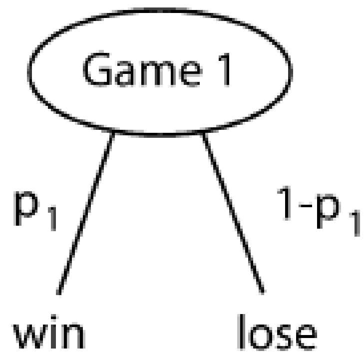
Both the ξ and δ alleles must be present for selection to act, otherwise neutral.

These are not unreasonable assumptions:

Selectively significant changes in expression are predicted (e.g., Stone and Wray 2001) and inferred (e.g.,Oleksiak et al. 2002) to be commonly occurring in natural populations.

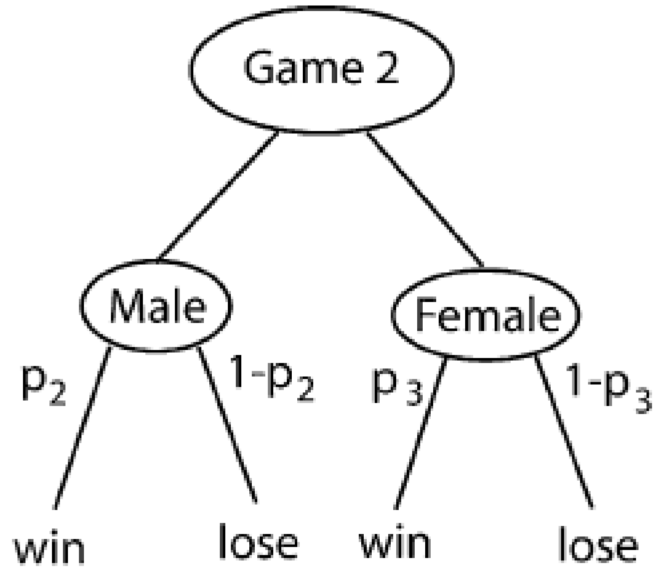
Furthermore, sexually antagonistic genetic conflict appears to be common in the genome, especially on the X-chromosome (e.g., Rice 1998; Chippendale et al. 2001; Gibson et al. 2002).

If the alleles do not occur in the same individual



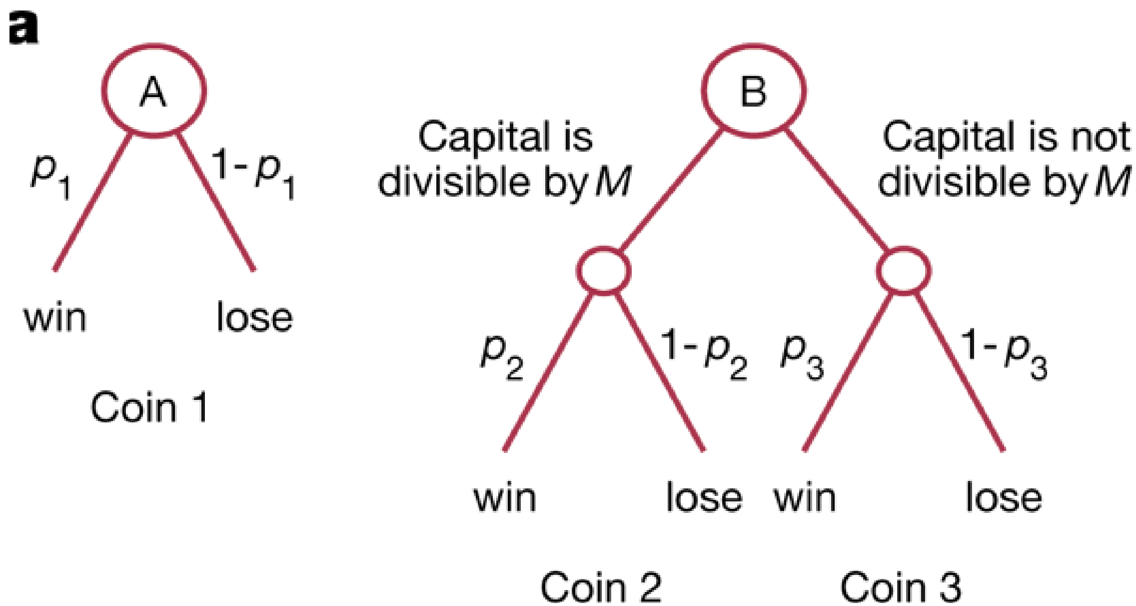
Neutrality
Fitness=1

If the alleles occur in the same individual



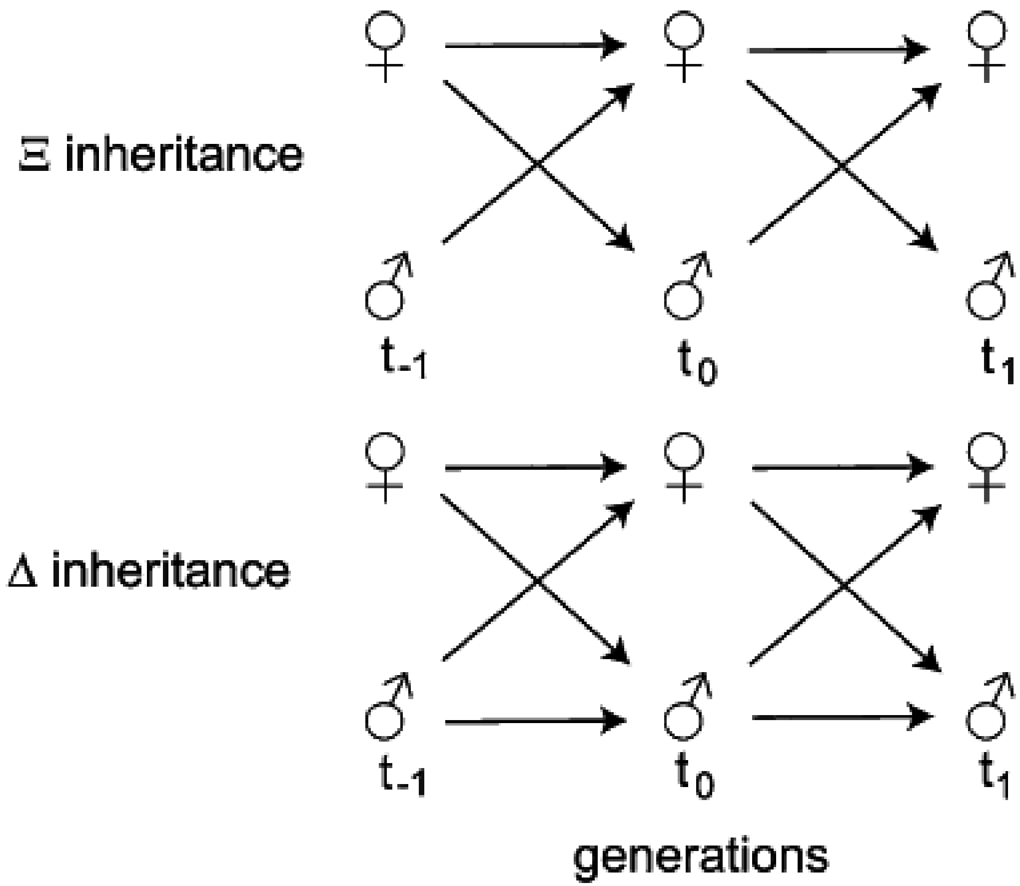
Antagonistic selection
Male Fitness=0.3
Female Fitness=1.5

Sex Averaged Autosome
Fitness =0.9



(Harmer and Abbott 1999)

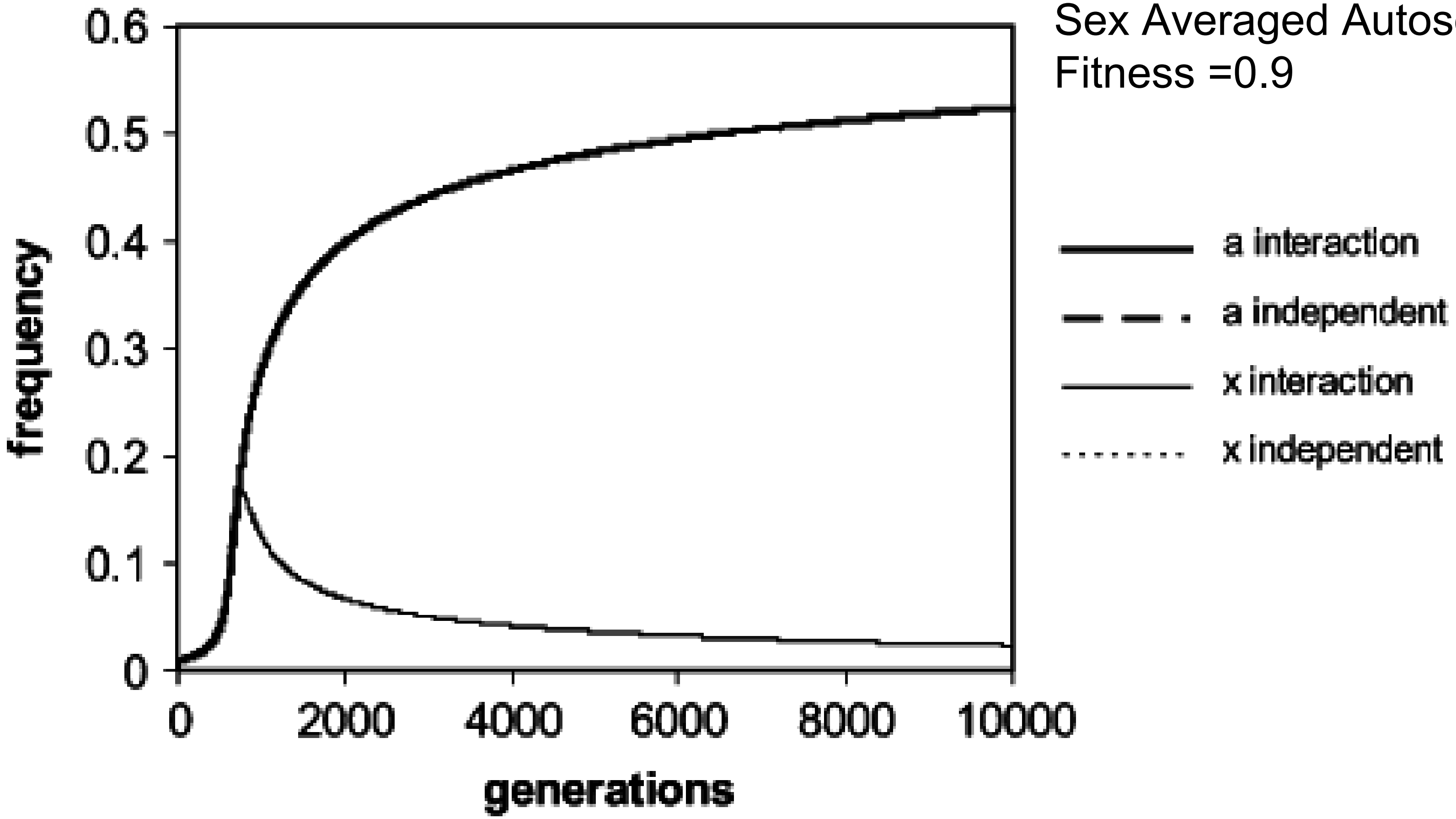
Inheritance pattern over time:



The allele frequency in each sex is a second order Markov-chain.

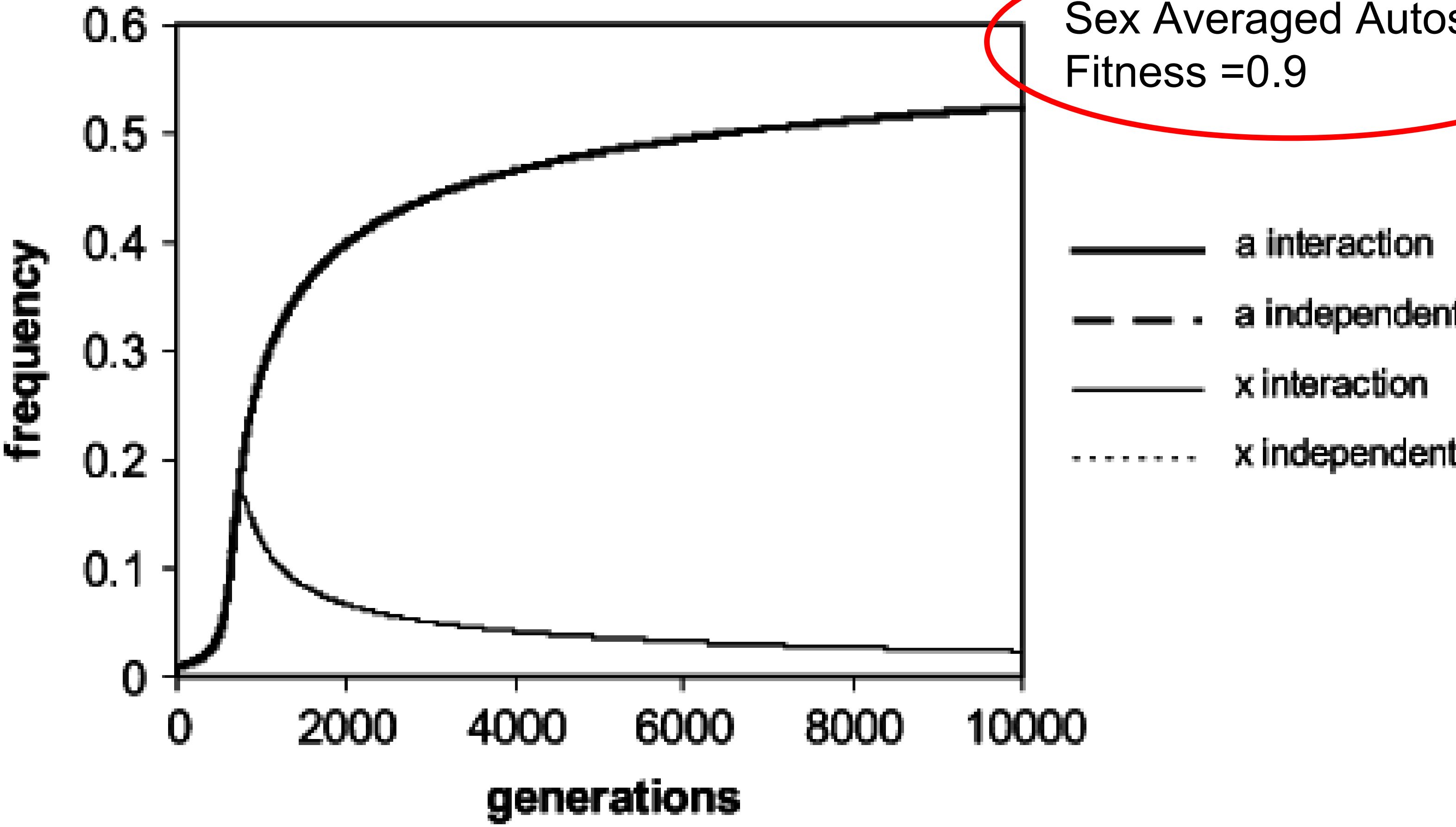
Antagonistic selection
Male Fitness=0.3
Female Fitness=1.5

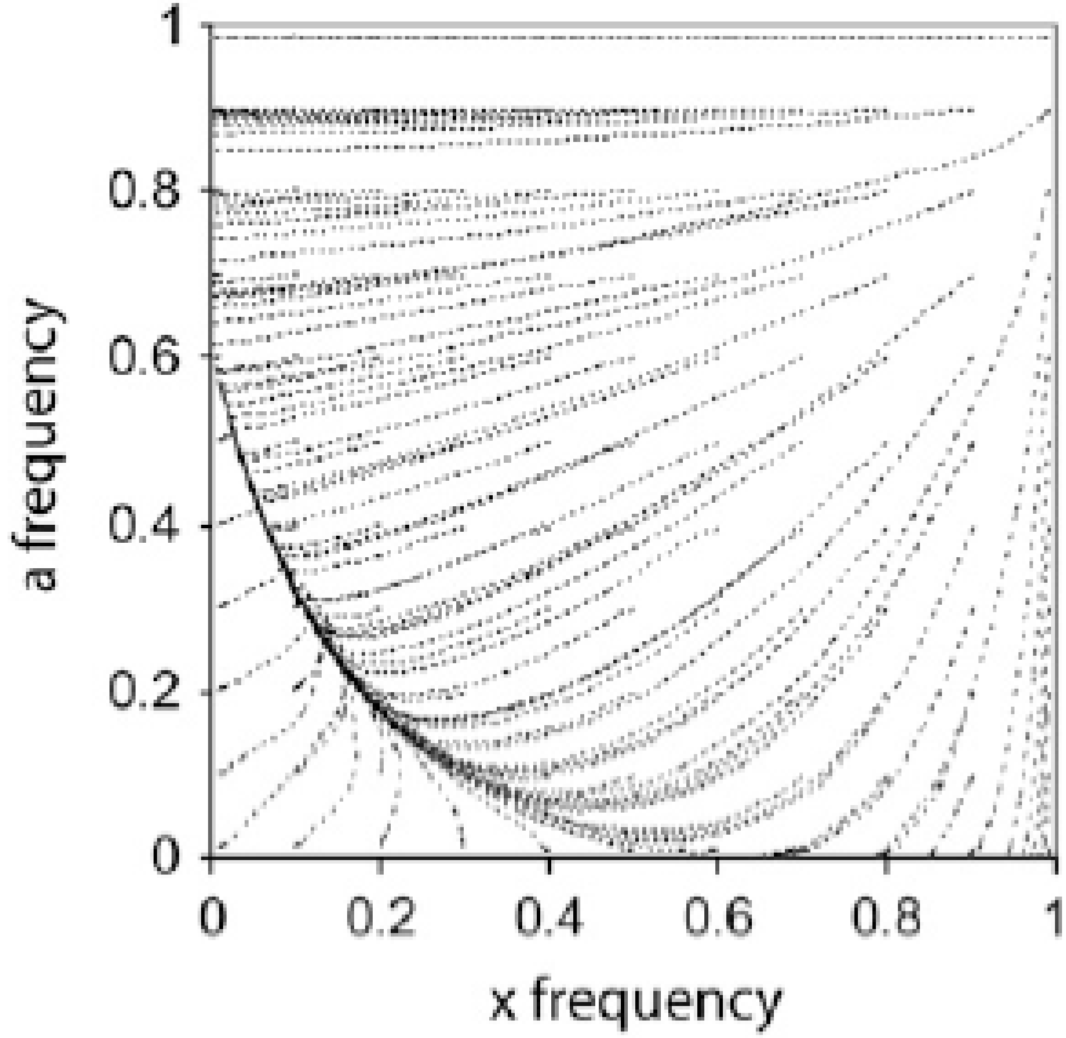
Sex Averaged Autosome
Fitness =0.9



Antagonistic selection
Male Fitness=0.3
Female Fitness=1.5

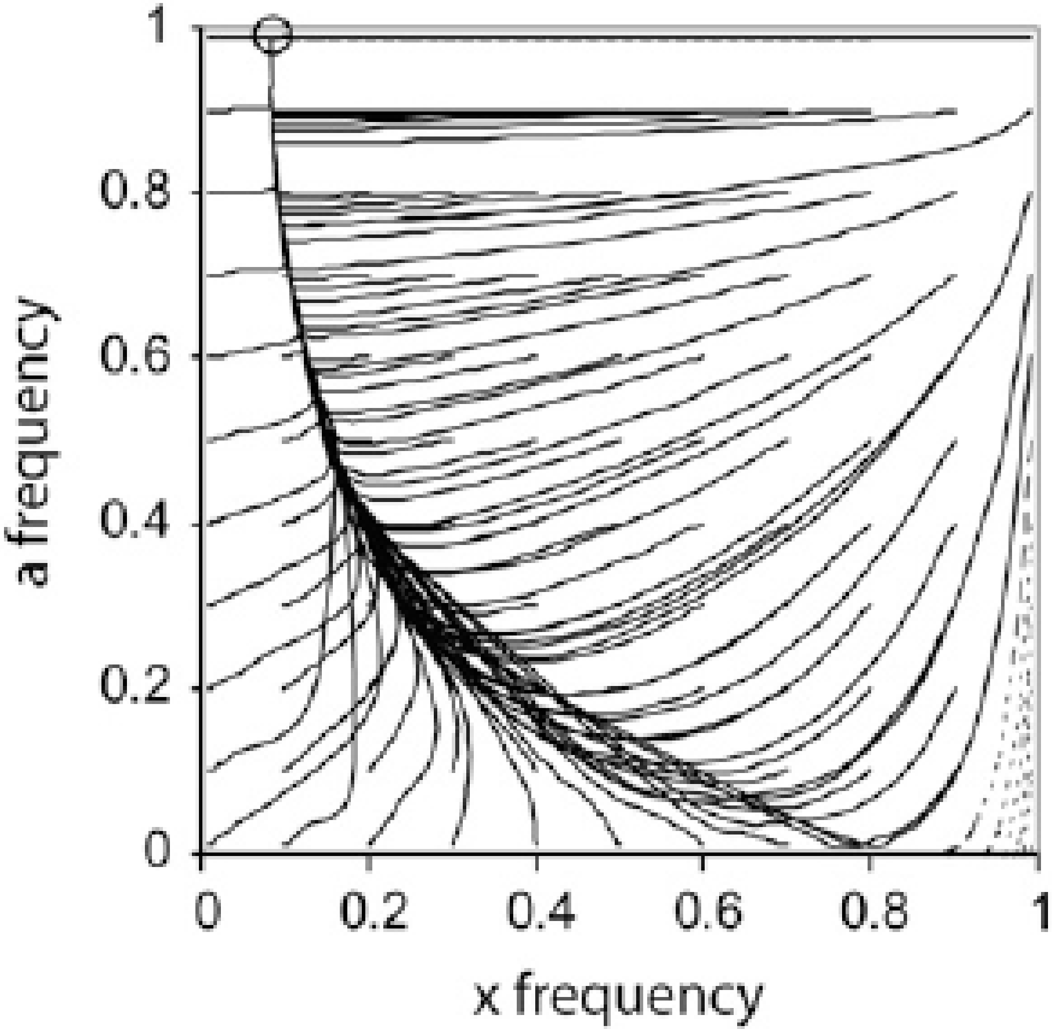
Sex Averaged Autosome
Fitness =0.9





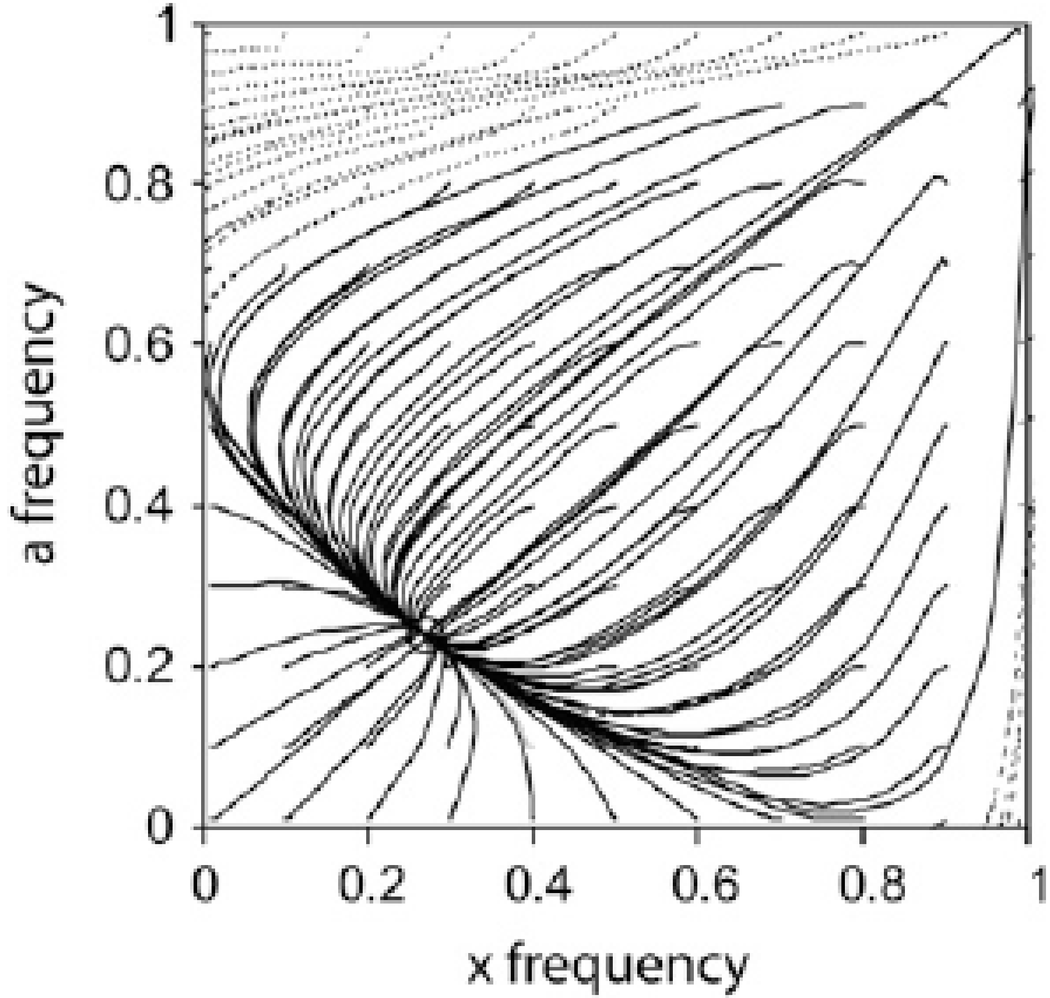
Antagonistic selection
Male Fitness=0.3
Female Fitness=1.5

Sex Averaged Autosome
Fitness =0.9



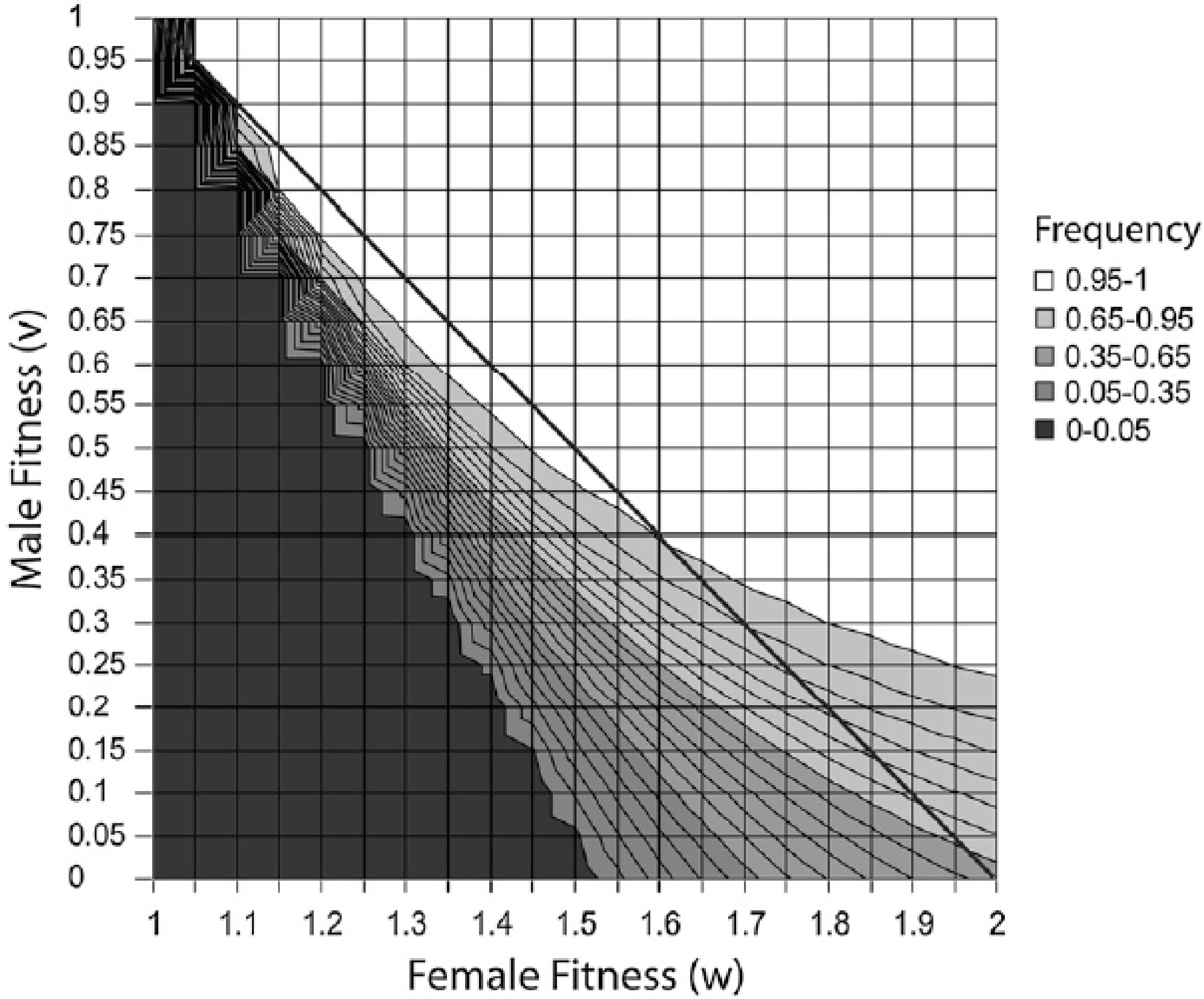
Antagonistic selection
Male Fitness=0.4
Female Fitness=1.5

Sex Averaged Autosome
Fitness =0.95



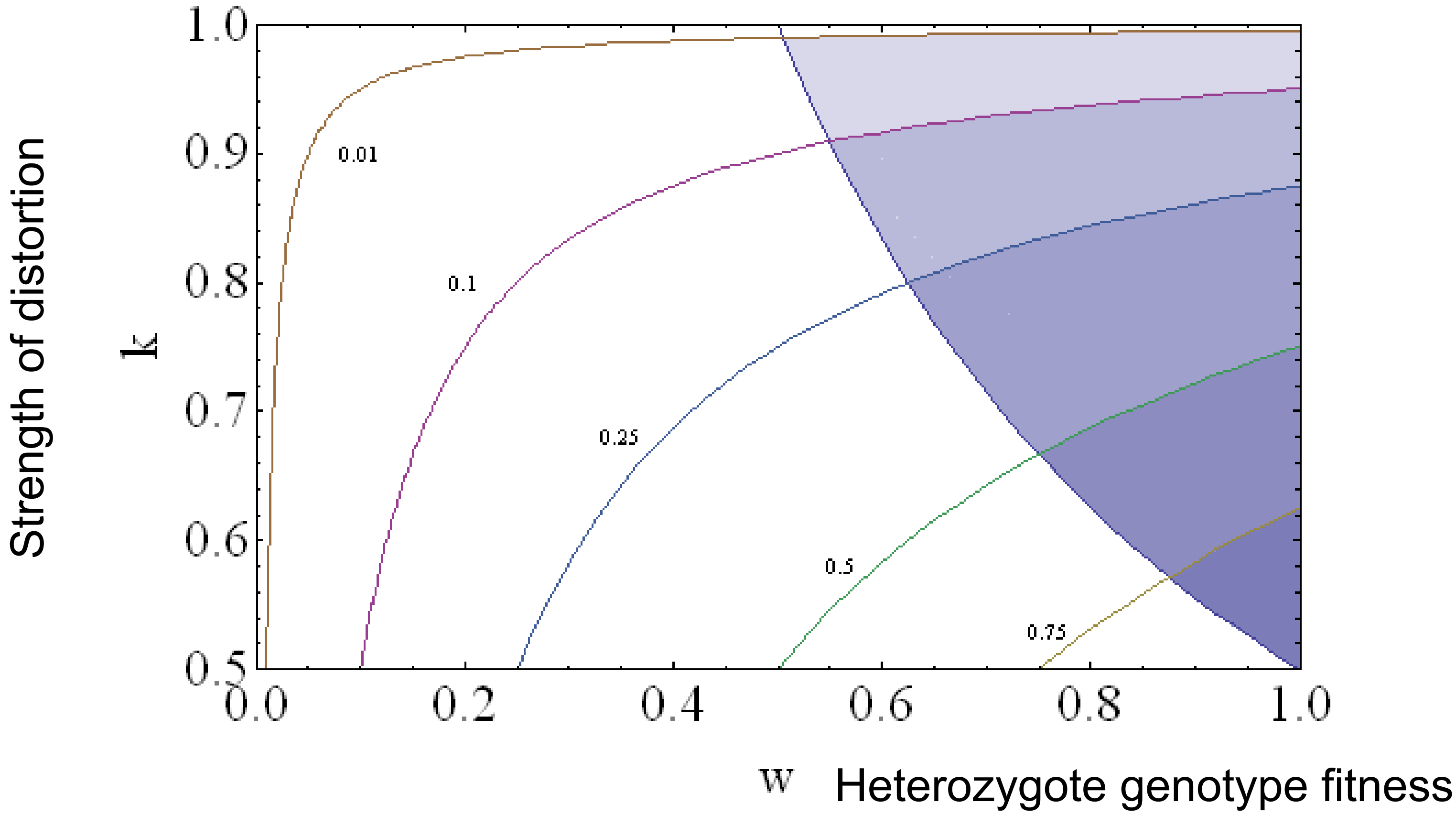
Antagonistic selection
Male Fitness=0.4
(het. 0.7)
Female Fitness=1.5
(het. 1.25)

A convex winning curve is necessary for Parrondo's paradox (Harmer and Abbott 2002).



“Non-adaptive” systems that can result in or mimic Selective sweeps

Meiotic Drive *
Parrondo’s Paradox
Underdominance
Background-selection
Hotspots of recombination



For a drive allele to invade the population, the *w*, *k* coordinate must be above the declining curve on the right; in this curve *w* refers to the heterozygous fitness. For the allele to fix in the population, *w*, *k* must be above the increasing curves, which are labeled by their homozygous fitnesses. A stable polymorphism is maintained in the shaded area between the curves.

Meiotic Drive

Genomes can adapt to meiotic drive by suppressing drive.

Drive may be uncovered by population crosses (because suppression and drive may be separated).

Evolution, 51(6), 1997, pp. 1886–1895

THE *SEX-RATIO* TRAIT IN *DROSOPHILA SIMULANS*: GEOGRAPHICAL DISTRIBUTION OF DISTORTION AND RESISTANCE

ANNE ATLAN, HERVÉ MERÇOT, CLAUDIE LANDRE, AND CATHERINE MONTCHAMP-MOREAU

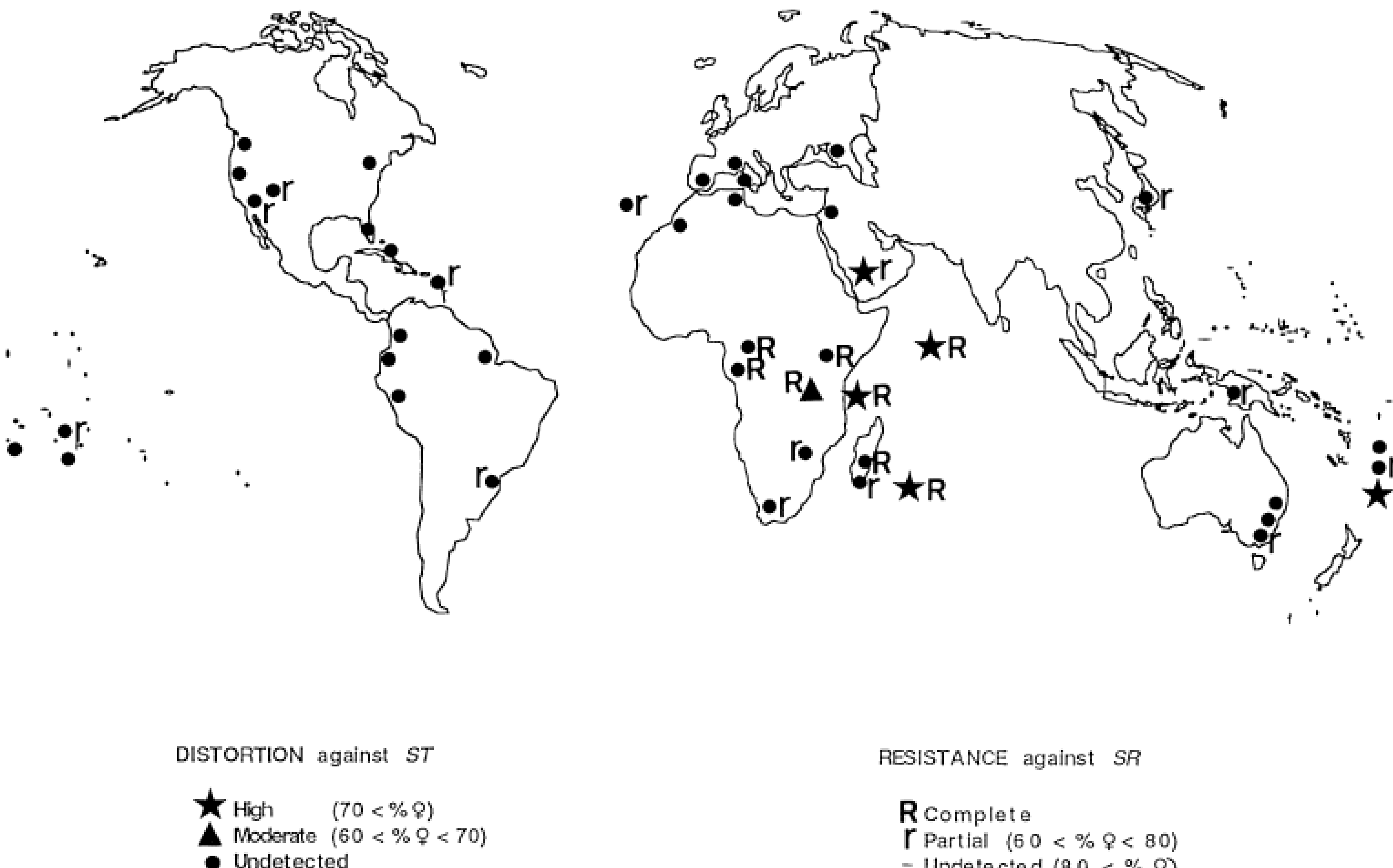


FIG. 3. Geographic distribution of the distortion and resistance factors. This figure presents the results of distortion and resistance tests (see Fig. 2) performed using mass crosses. Strains are presented in Table 1.

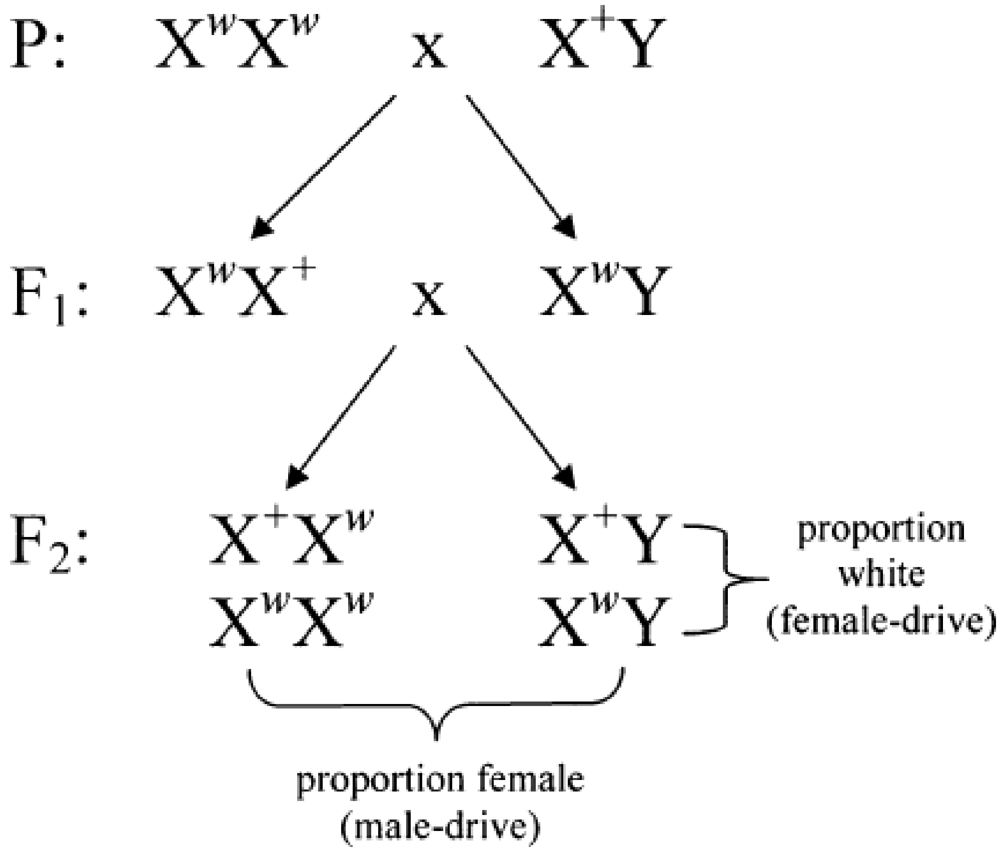


FIG. 1. The crossing scheme used to detect unequal inheritance of chromosomes from the hybrid F_1 parents. The proportion of white phenotypes in the F_2 offspring indicates the relative inheritance of the X-chromosomes from the female F_1 parent. The sex ratios of the F_2 flies indicate the relative inheritance of the sex chromosomes from the male F_1 parent.

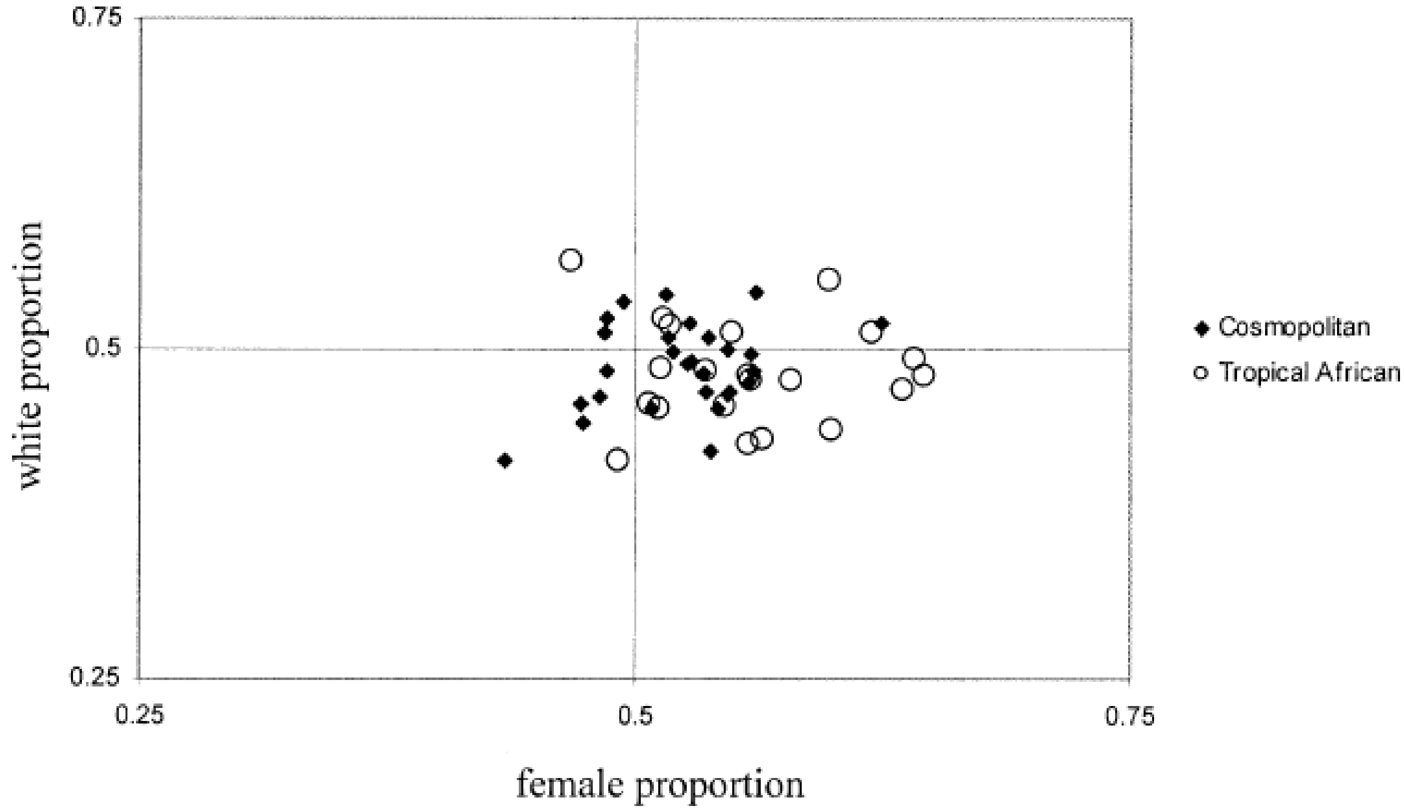
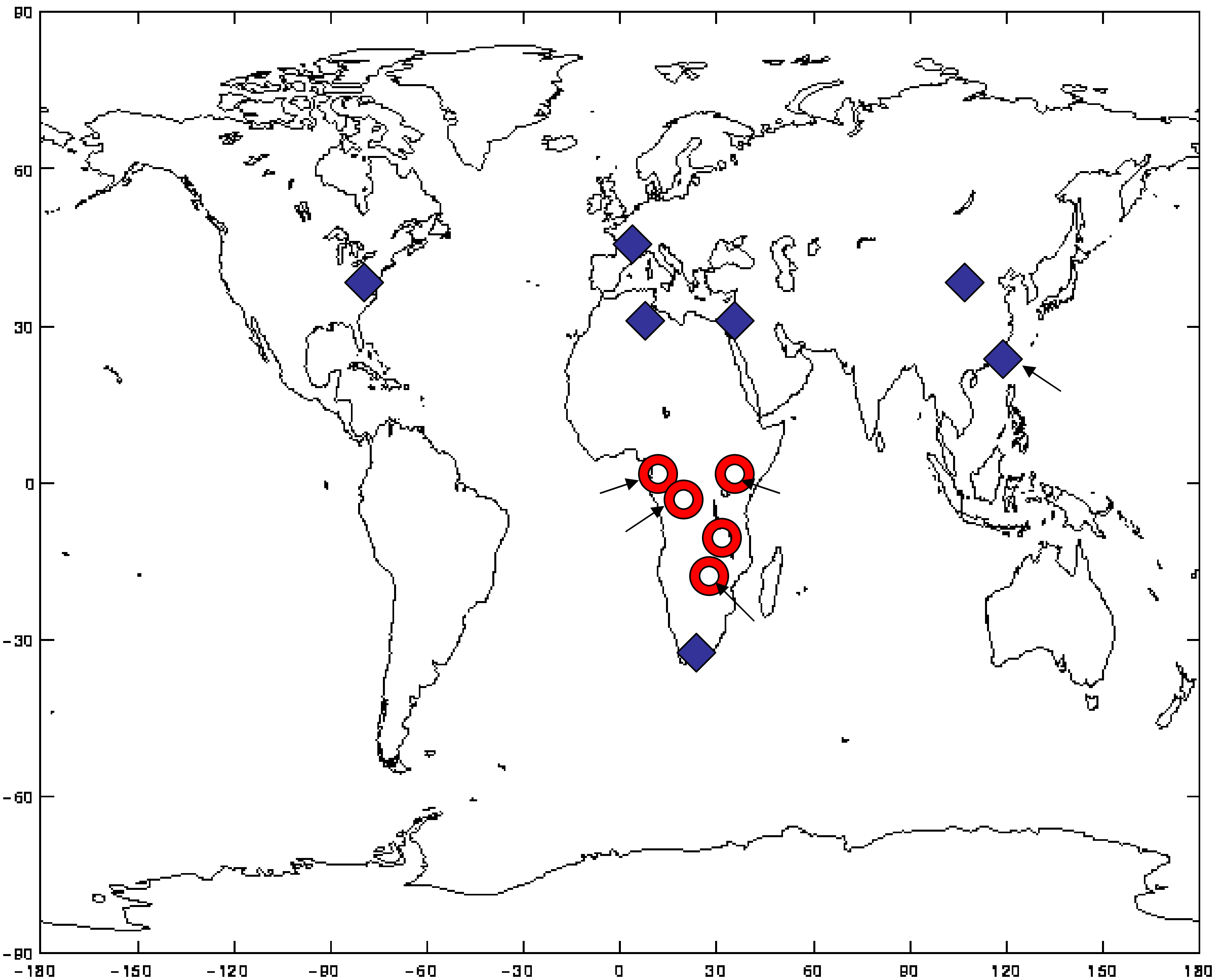


FIG. 2. Plot of the relative inheritance of chromosomes in 23,171 F_2 flies from crosses with 49 tropical African or cosmopolitan isofemale lines. The proportion of the white phenotype results from the relative inheritance of one of the two (*white* or wild-type) X-chromosomes from the hybrid female parent. The proportion of females results from the inheritance of either the X- or Y-chromosome from the male parent. The crossed lines indicate the null expectation of equal inheritance. For example, a female proportion greater than 0.5 is consistent with a driving X-chromosome in hybrid F_1 males; a white proportion of less than 0.5 is consistent with a driving X-chromosome in out-of-phase linkage between the drive element and *white* allele in hybrid F_1 females (see Fig. 1).



90
60
30
0
-30
-60
-90
-180
-150
-120
-90
-60
-30
0
30
60
90
120
150
180

Signatures of selection in hybrid lineages?

http://pond.dnr.cornell.edu/nyfish/Cottidae/slimy_sculpin.jpg

Caution in interpretations of selective sweeps

A selective sweep is not necessarily a result of adaptation that is beneficial to the organism (or even the fixation of a more adapted allele—from the alleles point of view) and may decrease organismal fitness.

“Non-adaptive” systems that can result in or mimic Selective sweeps

Meiotic Drive
Parrondo’s Paradox
Underdominance *
Background-selection *
Hotspots of recombination *

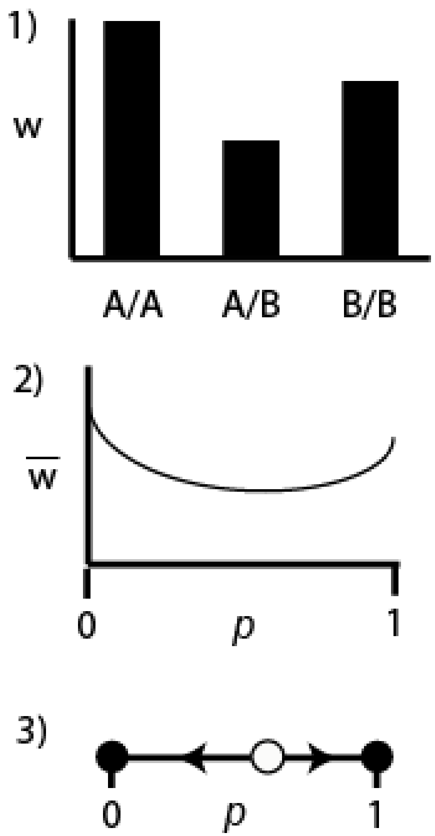
Thanks to

Guy Reeves
Diethard Tautz
Monday Theory Group
Aquavit Organizers

“Non-adaptive” systems that can result in or mimic Selective sweeps

Meiotic Drive
Parrondo’s Paradox
Underdominance *
Background-selection
Hotspots of recombination

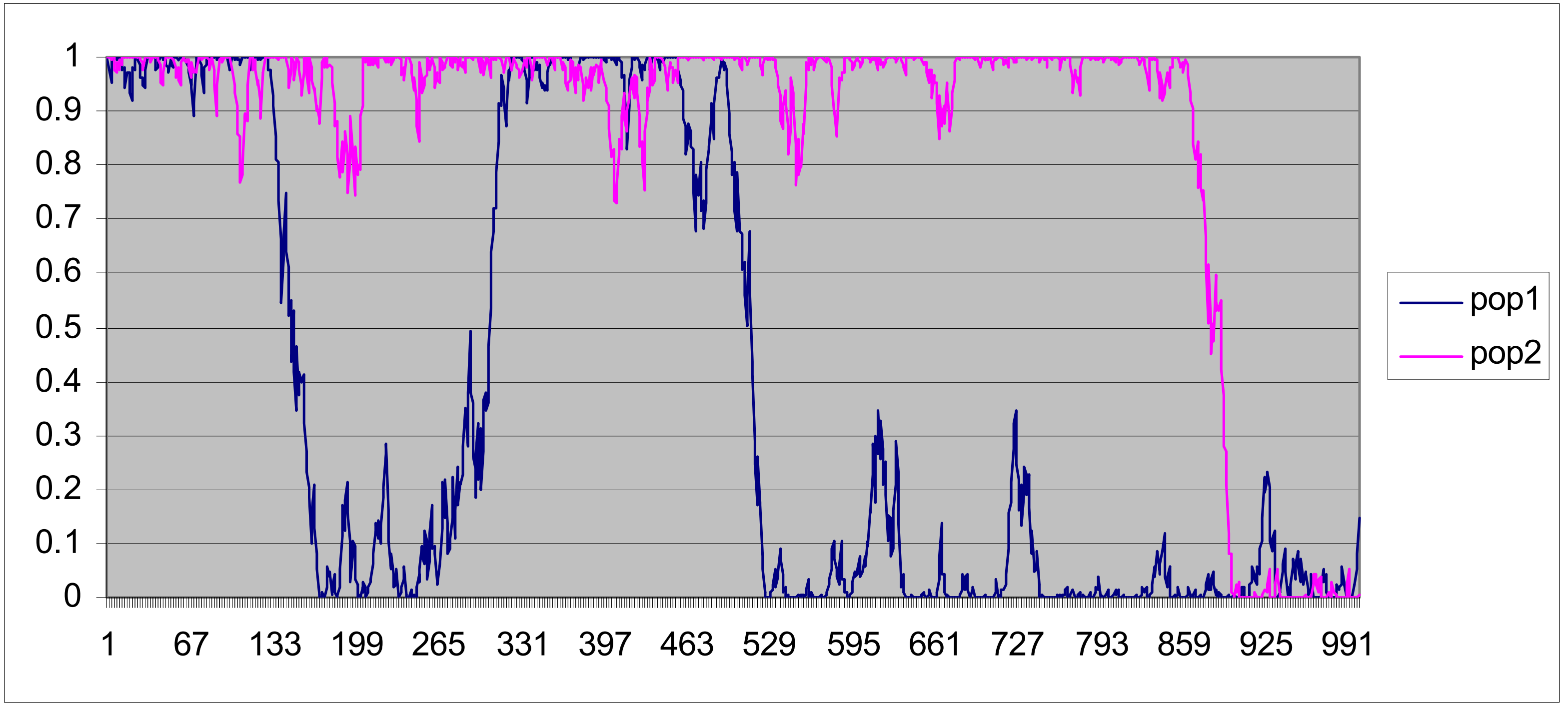
An Evolutionary Bistable Switch



- UD mutations can not increase when rare, but can go to fixation when starting at a frequency greater than the unstable equilibrium, $\hat{p}$.

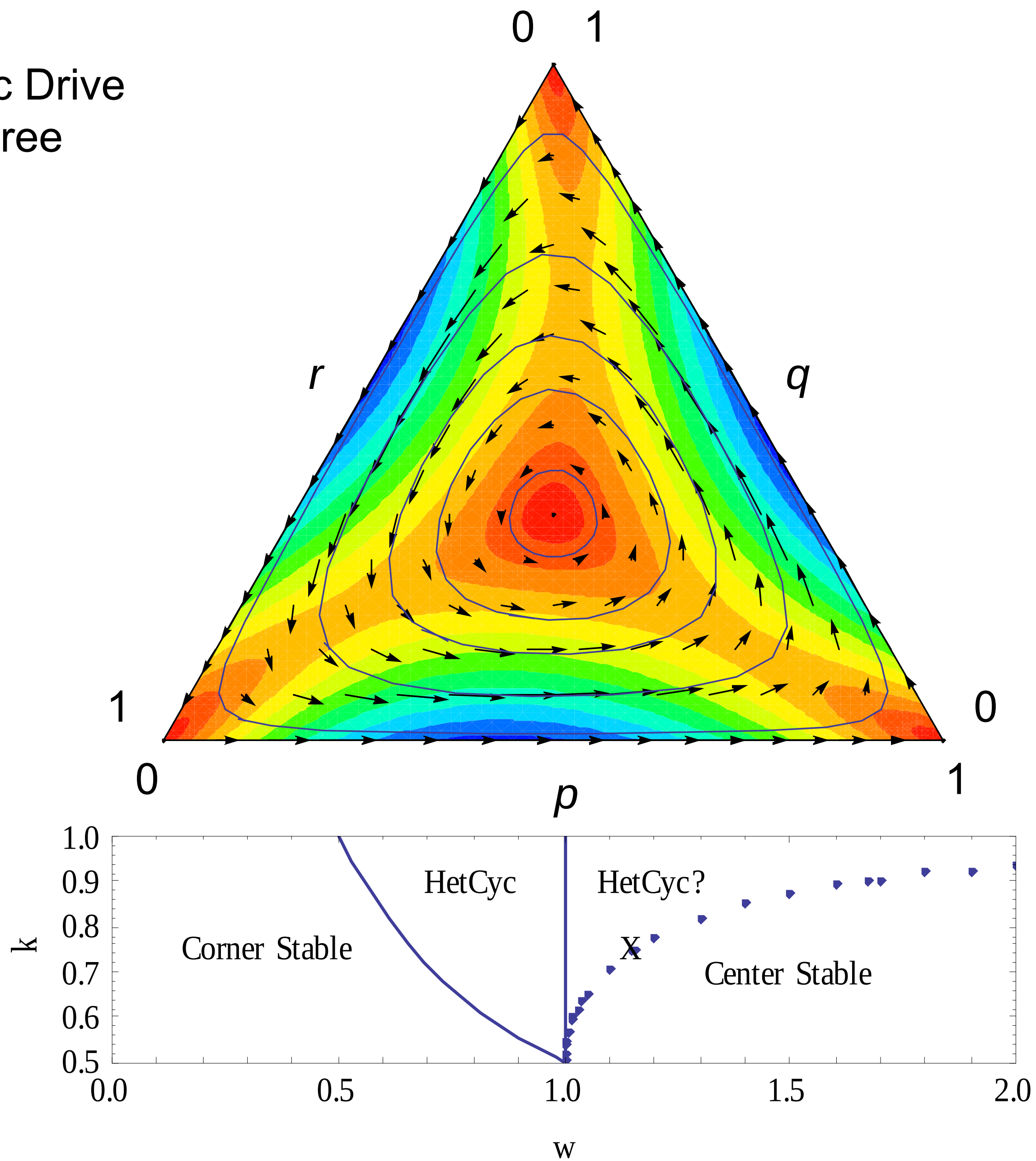
$$\hat{p} = \frac{w_{AB} - w_{BB}}{2w_{AB} - w_{AA} - w_{BB}}$$

With underdominance alleles can transit from low to high frequency by drift/selection, but this occurs rapidly—may affect linked variation.



Wh=0.95
m=0.05
N=20
L=200

Meiotic Drive with three alleles



Periods of apparent stability can suddenly give way to rapid sweeps.