Sex & Sex Ratio
Sexual vs Asexual Reproduction

• GOAL = produce offspring = fitness

• Asexual reproduction produces offspring with the exact copies of themselves (pass on copies of all its genes to the offspring)

• Sexual reproduction: two parents give rise to offspring that have unique combinations of genes inherited from the two parents

• Offspring of sexual reproduction vary genetically from their sibling and both parents
• Can look at modes of reproduction along a continuum:

Asexual (cloning)  Facultative sexual  Obligate sexual

Increasing degrees of genetic mixing
Importance of meiosis

- Meiosis keeps the number of chromosomes constant generation after generation.
- Without meiosis, the number of chromosomes would continue to increase each generation.
- Each generation (humans):
  1 sperm (23 chromosomes) + 1 egg (23 chromosomes) = 1 zygote (46 chromosomes)
- The new zygote grows by mitosis. Each new cell has 46 chromosomes.
Sexual Reproduction

MITOSIS
(a) Interphase
(f) Mitotic telophase
(b) Early mitotic prophase
(e) Mitotic anaphase
(c) Late mitotic prophase
(d) Mitotic metaphase

• Cloning
• For growth or repair

MEIOSIS
Meiotic Division 1
DNA Replication and Recombination
Cell Division 1
Meiotic Division 2
Cell Division 2

• Genetic mixing
• To produce sex cells
Genetic Mixing

- crossing over
- independent assortment
- fertilization
Sexual Reproduction

Sex is an evolutionary puzzle.

Associated Costs:
- Cost of Sex
- Cost of Meiosis
- Cost of Recombination
- Cost of Mating

Benefits must outweigh costs:
- Repair of damage DNA
- Reduce sibling competition
- Counter Muller’s Ratchet
- Counter the mutational deterministic process
- Adaptation in fluctuating environments
- Enhanced adaptation under directional selection
Two Fold Cost of Sex

- Two genotypes: 1 sexual, 1 asexual.
- Only half of the offspring of a sexual female will be female (an asexual female produces all daughters).
- Given equal fecundity to both genotypes, a sexual female has $\frac{1}{2}$ as many grandchildren as an asexual female.
- Thus, the rate of increase of the asexual genotype is ~ 2x that of the sexual genotype.

The *two-fold cost of sex*. If each individual were to contribute to the same number of offspring (two), the (a) sexual population remains the same size each generation, where the (b) asexual population doubles in size each generation.
Cost of Meiosis

• Non-sexual reproduction (cloning):
  • There is a probability of 1 that a particular gene ends up in a resulting offspring.

• Sexual reproduction with 2 sexes:
  • There is a only a probability of 1/2 that a particular gene will end up in a resulting offspring.

• Thus: A female could raise an offspring that carried all her genes but, with much more effort and much more cost, she rears offspring that only carry 1/2 of her genes.
Cost of Recombination and Segregation

- Recombination destroys adaptive combinations of genes at different loci (recombination load)
- Segregation destroys adaptive combinations of alleles within loci
- E.g. Heterozygote advantage of sickle cell anemia
  - aa = homozygous recessive = often lethal
  - AA = healthy but susceptible to malaria
  - Aa = little anemic but resistant to malaria

( Bharadwaj, 2006 ) Recombination load. If the two loci shown interact in their effects on fitness, such that allele A interacts well with B but poorly with b, and vice versa for a, the frequency of the double heterozygote AB/ab (in which recombination reduces the frequency of AB and ab) will be greater than that of Ab/aB (where recombination has the reverse effect) in a randomly mating population. Recombination will thus have the net effect of reducing the frequency of the favored gamete types, AB and ab, and so will reduce the mean fitness of an equilibrium population.
Cost of Mating

- Search costs, attracting a mate, etc
  - courtship takes time and energy
  - ornamentation
  - chemicals
  - competition with others trying to find a mate
    - mating during fertile time period
    - machinery required
      - special reproductive organs
- Risk of disease transmission
- Risk of not mating

Futuyma 2005
Benefits

I. Sex helps remove deleterious alleles
   • Repair hypothesis
   • Muller’s Ratchet
   • Kondrashov

II. Sex helps spread advantageous alleles
   • Fisher-Muller

III. Sex promotes genetic variability
Remove deleterious genes
- Repair of damaged DNA

- Sex evolved as gene repair mechanism
- If one allele damage, intact allele provides template for repair
- Meiotic recombination provides intact template to recover damaged information (but this is essential only for ds-breaks; which are induced by meiosis!)
- Sex provide intact copy from another individual
- Y-chromosome degeneration = recombination is needed for long-term fitness of large genomes
- But, relatives would have closest exact copies of alleles
- Yet mating among sibs is not very common
- Haploids don’t have spare copy to repair damage alleles, yet most haploids reproduce asexually (although parasexual genetic exchange does occur in most asexual organisms)
Remove deleterious genes
- Muller’s Ratchet

- Ratchet moves easily in one direction
- Asexual reproduction
  - Mutations accumulate easily but are not easily lost
- Ratchet more effective for species with many genes and small pops (humans vs bacteria)
- Recombination produces low-mutation classes and favorable combinations of alleles
  - Fewer mutations with fewer genes
  - Zero-mutation... category can be lost by drift
  - Mutations spread slower in large pops
- Fitness $\downarrow$ slowly under ratchet so sex advantage $<$ twofold cost of sex
- May explain longer-term survival of sexual lineages
  - Many abundant and small species reproduce sexually
Remove deleterious genes
Kondrashov

- A few mutations are tolerable
- Many mutations are not tolerable (cumulative effect)
- Combined mutations ↓ fitness (synergistic epistasis)
- Recombination exposes combined mutations to selection so they are purged in sexual populations
- Sex increases the variance in the # of mutations
  - Sex generates more individuals with fewer mutations via recombination
  - Individuals with many mutations die anyway
- Effective if deleterious-mutation rate is 1/G (counter 2x-cost of sex)
- Unknown if μ is high enough.
- Tests in E. coli don’t show predicted synergistic effect of deleterious mutations.

**Deterministic mutation hypothesis**

Different relationships between numbers of mutations and fitness. Kondrashov's model requires *synergistic epistasis*, which is represented by the red line - each mutation has a disproportionately large effect on the organism's fitness.
Remove deleterious genes

Otto & Gerstein 2006

Empirical data reports little epistasis with large variability among loci, which do not favor sex and recombination. Thus, negative epistasis is likely not an general explanation.

Figure 1 | Weak and negative epistasis is required for sex and recombination to be favoured

In a deterministic model where individuals with zero, one and two mutations have fitness 1, 1−s and (1−s)2 + e respectively, modifier alleles that increase the frequency of recombination (Rec) spread only when epistasis is negative and small relative to selection, s. The different isoclines correspond to the initial level of recombination within a fully sexual population. Figure produced from exact numerical results in [17]; similar conditions are observed when mutations are advantageous [10].
**Benefits**

**Increased Genetic Variability**

- Sex promotes genetic variability
- Hence, sex speeds up evolution
- Problems with this explanation
  - Requires sex to increase heritable variance in fitness
  - Recombination load
  - Segregation destroys favorable heterozygotes
  - Anisogamy increases cost of sex

Sex might create novel genotypes more rapidly. Two advantageous alleles $A$ and $B$ occur at random. The two alleles are recombined rapidly in (a), a sexual population, but in (b), an asexual population, the two alleles must independently arise.

In small sexual populations (4), however, the interval between the occurrence of favorable mutations is so long that a sexual population does not adapt more rapidly than an asexual population. (After Crow and Kimura 1965.)
Benefits
Sibling Competition

- If genotypes vary in their use of limiting resources
- Genetically identical siblings compete more intensely than sexual siblings
- Segregation & recombination can $\uparrow$ # of surviving offspring by $\downarrow$ sib competition or by $\uparrow$ prob of successful offspring
- But sib competition is restricted to some taxa (not a general explanation)
- This is an argument of selection at the level of individuals
Benefits
Adaptation to Fluctuating Environments

• Polygenic trait subject to stabilizing selection
  – Reduction of additive genetic variance
  – Negative linkage disequilibrium (selection for intermediate phenotype)
• Optimum trait changes due to environmental fluctuations
  – Selection now favors a new genetic combination which can easily arise in a sexual population but doesn’t exist in a sexual pop.

• Sex provides short- (> offspring) and long-term (higher rate of adaptation of populations) advantage over asexually reproducing
• Requires frequent environmental fluctuations
• Requires a factor maintaining genetic variation, for long-term stabilizing selection will fix a homozygous genotype.
  – Parasites?

\[
\frac{dw_{pop'n}}{dt} = V_G
\]

\[R = h^2 S\]

In response to environmental change,
- Sexually reproducing species will track the environment better.
- Offspring of parents with sexual reproduction will succeed better, on average, because they are more variable.

\[dw/dt = \text{the rate of change of mean population fitness}\]

Fisher’s Fundamental Theorem of Natural Selection
Benefits
Adaptation to Fluctuating Environments

- Resistant host genotype increases in frequency
- Parasite evolves to attack it
- Rare host genotypes acquire higher fitness = increase in frequency
- Coevolution favors sex as it produces rare host genotypes
  - Requires very strong S by parasites
  - P-H coevolution may not occur at time scale needed
- Perhaps not a general explanation but more data are needed

Figure 17.21 Evidence that selection by a parasitic trematode may favor sexual reproduction in a freshwater snail species that has both sexual and asexual genotypes. (A) The proportion of sexual genotypes is greater in local populations that are exposed to a high incidence of the parasite, as shown by the decreased proportion of females in such populations. (B) When snails of different asexual genotypes were exposed to trematodes, individuals with a rare genotype were less likely to become infected than were those with four common genotypes. (A after Jokela and Lively 1995; B after Lively and Dybdahl 2000.)

Futuyma 2005
**Benefits**

**Enhanced Adaptation Under Directional Selection**

- Sex enhances rate of adaptation to new environments by combining new mutations or rare alleles.
- Not true for small populations
- Tested in *Chlamydomonas* algae.
- Slow asexual adaptation likely a cause of frequent extinction
- DS infrequent = short-term advantage may not counter cost of sex.

**Figure 1** Effect of bottleneck size on adaptation in asexual populations. **a**, Individual points represent individual assays, and the different symbols indicate the lines from the initial four base populations. The relationship was examined statistically by fitting general linear models (GLM) to the data after log-transforming both variables. This has several advantages over using nonlinear regression on the untransformed data: the GLM framework means that line effects and line-by-population-size interactions can be fitted to the data as well as the population size term; and working with logarithms of population sizes reduces problems of leverage by the extreme population sizes. Initially I fitted both quadratic and linear population size terms, but the quadratic term did not significantly improve the fit, and so was dropped from the model ($F_{1,11} = 0.16, P = 0.69$). **b**, Overall pooled means and standard errors of the lines on an untransformed scale along with the fitted relationship from the GLM. On the untransformed scale the linear relationship takes the form adaptation $= b(Au)^2$, a relationship that is potentially able to describe the variety of relationships from diminishing returns to linear to accelerating. The actual fitted relationship is adaptation $= 0.00575$ (effective population size)$^{0.19}$, which is clearly of the diminishing-returns form. I chose a relationship that passes through the origin because a population of size zero is not expected to adapt.

**Colegrave 2002**

**Figure 2** Interaction between sex and bottleneck size. Bars show the mean relative fitness (± s.e.) of the sexual lines compared with their asexual controls. Sex has a greater positive effect in the populations that were bottlenecked the least.
Two levels

- Origin
- Maintenance
- Forces may differ at each level
- Slight advantage of sex could cause its evolution in organisms that lack a specialized gametes, whereas anisogamous sexual populations are easily invadable by asexual variants
- Maintenance of recombination does not require large selective advantage
  - Mutation reducing recombination is not automatically transmitted at a higher rate
- Genomic imprinting in mammals requires sex
- Asexual reproduction in vertebrates (parthenogenesis) has evolved independently multiple times.
Sexes defined by gamete size (large = eggs, small = sperm)
Anisogamy = unequal gamete size
Anisogamy evolves if one genotype is favored because the large size of its gametes ↑ offspring survival, and another genotype is favored because it can make many gametes
Intermediates enjoy neither advantage
Hermaphroditism, dioecy
Sex ratio under dioecy ~ 50:50
Sex ratio allocation theory
Energy allocation of potential hermaphrodite: Male or female functions

Dioecy: allocation of 100% energy to one sexual function or the other

Shape of tradeoff: cost of developing structures for sexual functions

If structures are shared by sexual functions = hermaphroditism

If unique structures needed: dioecy favored (hermaphroditism too costly)
Sex Ratio

- Population sex ratio (PSR).
- Individual sex ratio (ISR): sex ratio in the progeny of an individual female.
- Selection favors equal parental investment in male and female production, and if the costs of producing one male and one female are identical, the sex ratio tends to equality (Fisher 1930).
- In a large, randomly mating pop with female sex bias, a genotype with male-biased ISR is favored because each individual of the minority sex has > # offspring than each individual of the majority sex (frequency-dependent selection).
- A genotype with ISR of 0.5 is an ESS (evolutionary stable strategy).
- ESS: if all the members of a population adopt it, no mutant strategy can invade via nat. sel.
- A population is in ES state if its genetic composition is restored by selection after a (not too large) disturbance.
Sex Ratio

- When the costs of producing a son and a daughter differ, a biased sex ratio can equalize total parental investment in male and female production, yield a higher reproductive success than the average under balanced sex ratios, and thus be selected (Shaw and Mohler 1953).
- Sex ratio will be biased towards the cheaper sex, or the sex with higher mortality (lower viability) (Fisher 1930)

\[ C_m \text{ can now be defined as the expected fraction of genes going from P to } G_2 \text{ contributed by a single male in P.} \]

\[ P = \text{parental generation} \]
\[ G_2 = F_2 \]

**Figure 2.** Genetic contribution of a male as related to \( x \), the sex ratio of his progeny, and to \( X \), the sex ratio of the population.

**Sex ratio = % males**
Sex Ratio

- Non-random mating, local group structured pop (progeny of a few ♀ emerge and mate, then the ♀s disperse (results in ♀-biased sex ratios)
- Example of Local Mate Competition (Hamilton 1967): ♂s compete for mates within groups (only few ♀s needed).

![Diagram](image_url)

**Figure 17.23** A model of the evolution of a female-biased sex ratio in a population that is structured into local groups, but periodically forms a single pool of dispersers. The frequency of $A_1$, an allele that biases the individual sex ratio toward daughters, is indicated by the dark portion of each circle. The size of each circle represents the size of a group or population. From a genetically variable pool, groups are established by one or a few founders. The frequency of $A_1$ varies among groups by chance. Although $A_1$ declines in frequency within each group over the course of several generations, the growth in group size is greater the higher the frequency of $A_1$ (because of the greater production of daughters). When individuals emerge from the groups, they form a pool of dispersers, in which $A_1$ has increased in frequency since the previous dispersal episode. (After Wilson and Colwell 1981.)

The $A_1$ allele biases the individual sex ratio toward daughters.

Within each group, $A_1$ declines in frequency, and the group evolves toward a 1:1 sex ratio.

$A_1$ has increased in the gene pool because groups with higher frequency of $A_1$ are more productive.

From a genetically variable pool, groups are established by $N$ founders.
**Sex Ratio**

- *Nasonia vitripennis*: progeny of 1 or >1 ♀ emerge and mate
- Females expected to produce more daughters than sons
- Sex ratio (%♂ expected to ↑ with # families developing in a host)
- If ♀ can detect she is 2nd at host, her sex ratio should be more ♂-biased

*Figure 17.24*  Adaptive adjustment of individual sex ratio by a parasitoid wasp in which females usually mate with males that emerge from the same host. The points show the relationship between the proportion of sons among the offspring of a “second” female (i.e., one that lays eggs in a fly pupa in which another female has already laid eggs) and the proportion of her offspring in the host. The curved line is the theoretically predicted individual sex ratio in second females’ broods, as a function of the sex ratio in the first female’s brood and the relative number of the two females’ offspring. If the second female’s offspring made up only a small fraction of the total, that female’s optimum “strategy” should be to produce mostly sons, which could potentially inseminate many female offspring of the first female. As predicted, the fewer the progeny of the second female, the more of them are sons. (After Werren 1980.)
Genotypic Sex Determination

Zygote → development → SEX

Genotype

XX → Hot → female

XY → Cold → male

GSD
Environmental Sex Determination

Zygote $\rightarrow$ development $\rightarrow$ SEX

Genotype

Environmental temperature

ESD, TSD
Vertebrates


<table>
<thead>
<tr>
<th>Category</th>
<th>GSD</th>
<th>TSD</th>
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<td>GSD</td>
<td>TSD</td>
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<td>Amphibians</td>
<td>GSD</td>
<td>GSD+EE</td>
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<td>Mammals</td>
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## TSD in Invertebrates

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<td>Insecta</td>
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Reviewed in Koperlainen 1991
# TSD in Plants

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<th>Pteridophyta</th>
<th>Spermatophyta</th>
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<td>• Zea mays</td>
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</table>
Heteromorphic sex chromosomes?

Yes

Sex ratio 1:1

No

Incubation at wide range of temperatures

Sex ratio not 1:1

TSD OR GSD + Environmental effect

Differential embryo mortality (resorption/abortion)?

Yes

Differential fertilization?

Yes

Sex reversal?

Yes

No

GSD

GSD + Environmental effect

TSD

Valenzuela et al. 2003, American Naturalist
Evolution of Sex Determination

Fig. 2. Regulatory cascades in *D. melanogaster* and mammalian sex determination involve factors acting upon pre-mRNA splicing. In the fly (left) SXL positively regulates TRA expression and downregulates MSL-2 in female flies. TRA-TRA2 heterodimers trigger expression of the female-specific DSX² isoform. In the absence of SXL, males express DSX². In mammals (right), WT1 (+KTS) isoforms upregulate Sry in the developing male gonad. Sry, in turn, negatively influences the expression – or the function – of an unknown Z gene, which inhibits testis differentiation genes. Z gene candidates are indicated (pink box).
Evolution of Sex Determination

SDM - Insects

Y-chromosomal genes (*Tipulidae, Tephritidae*)

Autosomal genes (*Culex, Anopheles*)

Mobile genes (*Megaselia, Musca*)

X:Autosome ratio (*Drosophila*)

Genotype of the mother (*Chrysoma, Sciara*)

Haploid/ diploid (*Hymenopterans*)

Environmental factors (*Pseudacteon*)
Evolution of Sex Determination

Figure 2. Variation in model system sex determination. Though mammals, Drosophila, and C. elegans all use GSD, they interpret their sex chromosome content through distinct signal transduction pathways. However, all three eventually converge on a DM family member whose expression is associated with male development. Drosophila Dsx is unusual for DM genes in also having an important role in female development (through a female-specific splice variant).

Figure 3. Models for germline sex determination in C. elegans and C. briggsae. (A) C. elegans, and (B) C. briggsae. In both panels, arrows indicate positive regulation, and crossbars indicate repressive regulation. With the exception of fog-3, the genes in black type are also crucial in somatic sex determination. Mechanisms promoting the initiation of hermaphrodite spermatogenesis are colored green, and those promoting the switch to oogenesis are colored red. Though it is likely that C. briggsae hermaphroditism is controlled by genes regulating the core pathway downstream of the Cb-fems, their identity is unknown.
Evolution of Sex Determination

Neuwald et al. in review
Evolution of Sex Determination

Valenzuela and Adams 2011, Evolution