BIOL2007 CHROMOSOMAL EVOLUTION

Why the location of genes matters

Genes are found on chromosomes. Rule: Gene action usually independent of chromosomal location.

> Exception 1: *position effects*. For example, *Hox* genes in clusters in orders that reflects order of segments in the body that they control. Suggests functional reasons.

Nonetheless, success in much genetic engineering implies that position often unimportant.

> Exception 2: Tight linkage may also influence evolution. With tight linkage and *epistasis* this may lead to linkage disequilibrium. With epistasis or linkage disequilibrium, genes do not act independently.

But again, maybe a relatively trivial effect, at least without strong epistasis like that in *Papilio*.

Significant linkage disequilibria present over very tiny, essentially intragenic, distances in eukaryotes, say <1 Mb in humans, and <100 Kb in *Drosophila melanogaster.*

However, the fact that genes are on chromosomes influences evolution far beyond the minor effects of position effects and linkage disequilibria.
Because the genes are arranged on long strings, and because chromosomes themselves act as genetic elements:-

Selection can act on 100s to 1000s of genes at a time.

Evolutionary oddities about chromosomes

Although we understand some of the processes involved in chromosomal evolution, we understand by no means all of them. (See Hartwell et al. in reference below).
Chromosome number, for example, varies enormously from organism to organism.

> In *Drosophila melanogaster*, there are only 4 pairs of chromosomes (*n = 4, 2n = 8).* Of these, one pair is a micro-chromosome which has hardly any genes on it; one pair is a sex chromosome, which leaves only 2 active pairs of autosomes.
>
> In humans, there are 23 pairs (*n = 23, 2n = 46*) chromosomes. Mammals in general are highly variable in chromosome number.
>
> Across the whole Lepidoptera, a group of similar age to the mammals, there is quite a bit of variability (10-100s!), but there is a strong modal number which many species in different groups of Lepidoptera actually have, of *n = 31*.

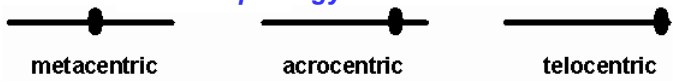
What explains these patterns?

It is not entirely clear. There is usually about one chiasma (causing a crossover) per chromosome arm; perhaps, therefore, chromosome number (like sex) is an adaptation which affects the general level of recombination in the genome.

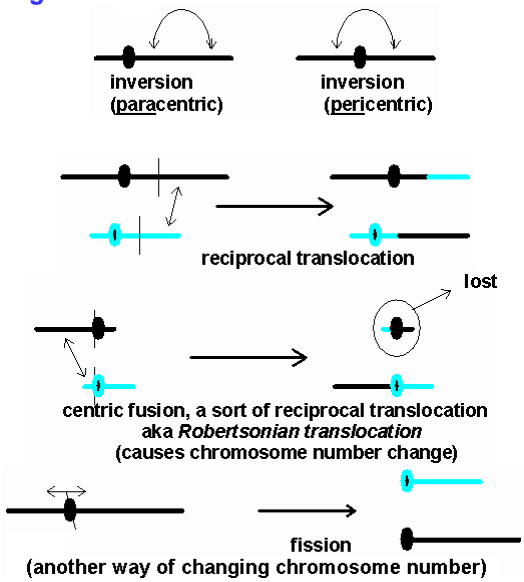
Many chromosomes means lots of of recombination (50% recombination between chromosomes, plus a lot of chiasmata); few chromosomes means little recombination.
But before we explore "why?" questions; here is a bit of terminology:

Chromosomal rearrangements are gross changes in chromosomal morphology. Lots of Greek: Telomere, centromere, autosome, chromosome, ...

Chromosomal morphology



Rearrangements



Instead of ***genotypes***, chromosomes have ***karyotypes***. Typically, karyotype means the number of chromosomes in a set, for instance, "*the human karyotype is 2n = 46*".

Polyploidy. Common chromosomal mutation involving a doubling of numbers of copies:

> *autopolyploidy* (doubling of endogenous chromosomes);
> *allopolyploidy* (hybridisation → doubling)

Abnormal numbers, a single chromosome pair adds more copies (*aneuploidy*); rare, leads to unbalanced gene dosages and sterility. Can you think of any aneuploidy in *humans?

Autopolyploidy and *allopolyploidy* particularly popular in flowering plants (30% of flowering plant species are of polyploid origin).

Probably because many *monoecious* and *hermaphrodite* plants can self. An autopolyploid branch or a new and rare allopolyploid can mate with itself, forming offspring with fully balanced gametes.

If a polyploid mates with a normal diploid, the F1 hybrid is triploid; this causes massive amounts of aneuploidy in the offspring, leading to almost invariable sterility of hybrid offspring.
So polyploidy can lead to speciation.

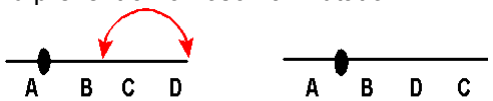
How do rearrangements occur?

Chromosome breakage. Can occur via radiation, mutagens etc. Repeated sequences, often transposable elements, in the DNA may frequently be involved, i.e. non-homologous recombination

> e.g. P- elements are involved in chromosomal mutation in *Drosophila*.
> *Alu* elements probably do in mammals; perhaps in us?

Breakage leads to "sticky ends" (? something to do with the function of a ***telomere***? See Hartwell et al.).

One of the telomere's functions is to "cap" the sticky ends, and prevent chromosomal mutation.



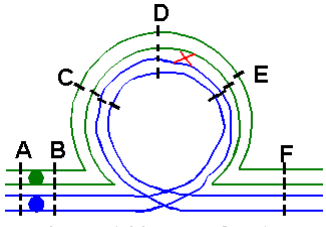
telomeric inversion

Telomeric inversions (where the telomere sticks to a breakpoint, as in the diagram above), are rare.
Most inversions instead are paracentric or pericentric; reciprocal translocations also preserve the telomere, and are common too.

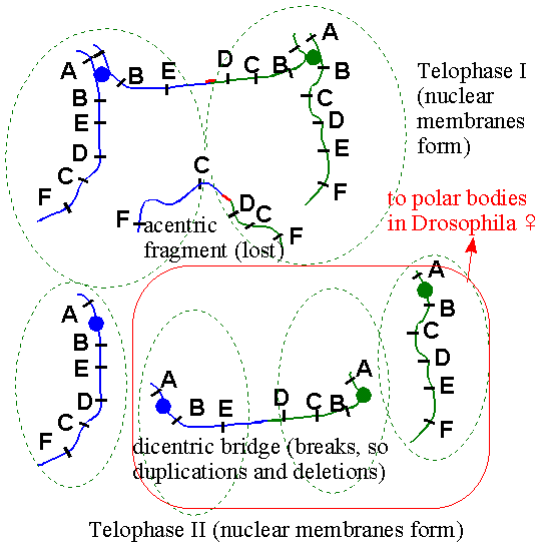
Evolutionary effect of rearrangements

General rule:
Heterozygous rearrangements often lead to the production, in meiosis, of UNBALANCED GAMETES;
often, **HETEROZYGOTE DISADVANTAGE**

e.g. ***Paracentric inversions***



Prophase I (chiasmata form)



Telophase II (nuclear membranes form)

If no crossing over in inversion: gametes fine
If crossing over in inversion, possible problems.

dicentric bridge (breaks at cell division)
acentric fragment (lacks centromere, becomes lost)

duplications and deletions of chromosomal material
→ developmental problems result.

Because a paracentric inversion heterozygote produces unbalanced gametes, the rearrangements cause:
heterozygote disadvantage → fixation

Because the deleterious effects act only if there is a crossover within the inversion of an inversion heterozygote, the inversion can acts as a ***crossover suppressor***: any crossovers that are produced become involved in unbalanced gametes and are lost. Only non-crossed-over chromosomes have normal fitness and survive.

However, little heterozygous disadvantage in *Drosophila* and many other Diptera (flies). Here, paracentric inversions are common, even within populations.

> In males, there is no crossing over, so no unbalanced gametes.
>
> In females, dicentric fragments are preferentially shunted into polar bodies.
>
> Mainly balanced gametes are found in the eggs.
>
> Thus, little heterozygote disadvantage. But plenty of crossover suppression.

Pericentric inversions

> Like paracentric inversions, only worse.

Reciprocal translocations

If no crossing over: approximately 50% (or more) unbalanced gametes due to *non-disjunction*, or non separation of homologous chromosomes

If crossing over: similar problems

Because paracentric inversion and translocations heterozygotes produces such unbalanced gametes, the rearrangements cause ***heterozygote disadvantage*.**

***Translocations are common in mammals*.**

Usually, populations are fixed for a translocation, as expected from the deleterious effects on gametes.

Populations fixed for alternative chromosomal rearrangements are often called *chromosomal races*. They are common in species such as the european house mouse *Mus musculus domesticus.*

However, non-disjunction rates are often low, 0% - 15%, not usually the approx. 50% that simple theory would lead one to expect.

Mammals, like *Drosophila*, appear to have mechanisms which reduce production of unbalanced gametes.

Evolution of sex chromosomes

(fascinating, but no time!!)

Evolution of paracentric inversions

Paracentric inversions are commonly polymorphic in Diptera.

There is even evidence for *HETEROZYGOUS ADVANTAGE*, which, as we have seen, will maintain polymorphisms. This is found in flies such as *Drosophila*, and also the malaria carrier, *Anopheles* mosquitoes. Why? Dobzhansky in 1930s suggested that inversions trap "coadapted gene complexes", groups of genes that interact *epistatically* in a positive way, having been built up by selection.

Dobzhansky: cyclical fluctuations of chromosomal polymorphisms with season; different forms favoured at different altitudes.

Proves chromosomal arrangements adaptive. But not why. Why heterozygous advantage?

Could be genic (e.g. *balanced deleterious recessive genes* on each chromosome).

Or could involve epistatic groups of genes that work together.

Phylogeny from rearrangements

Many chromosomes are morphologically differentiated enough, if stained appropriately, that chromosomes or parts of chromosomes can be clearly identified.

In humans/apes, chromosome banding patterns first showed that chimps are more closely related to humans than gorillas.

For *Drosophila*, phylogenies based on chromosmal inversions visualised via polytene chromosomes are very commonly used. Here's how:

(demonstrate in class)

However, DIRECTION of evolution cannot be inferred; the tree not easy to “root”.

For that, we need to find a good estimate of the primitive state. This is sometimes done by finding an OUTGROUP, which is close to the primitive pattern Sometimes by assuming that a particular form is primitive based on distributional or other data.

"Karyotypic orthoselection"

Similar repeated change happens in many chromosomes at once. The phenomenon is very interesting, but has not been fully explained.

For example, the primitive chromosome number of chromosomes in *Mus musculus domesticus*, the house mouse, is 2n = 40, all acrocentrics. However, by a series of Robertsonian fusions, there are multiple chromosomal races with less, some of which have as few as 2n = 22. Nobody knows why.

Evolutionary significance

Heterozygous disadvantage *may prevent evolution of new chromosome rearrangements*

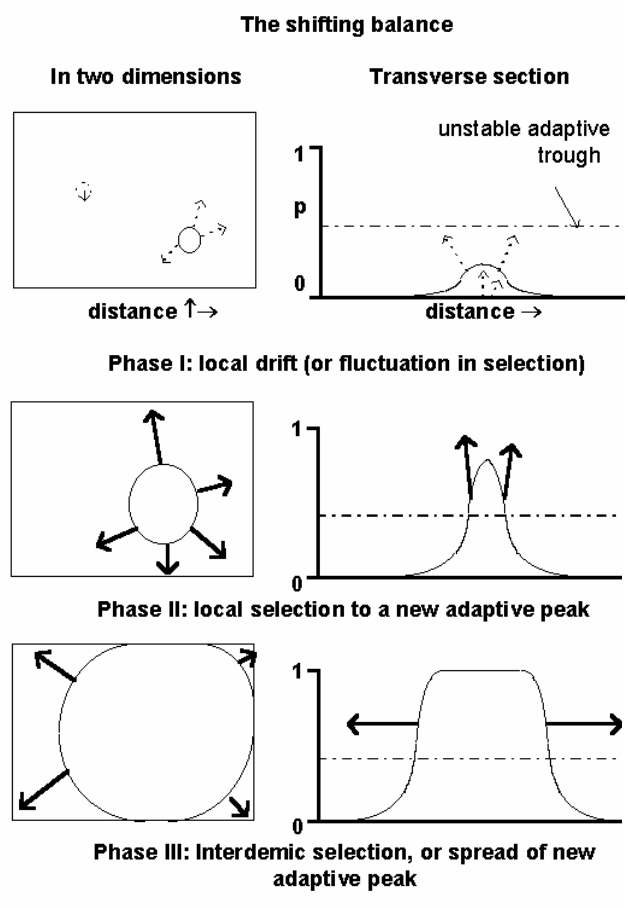
Most populations should be fixed for chromosomal rearrangements. In general, this is true.

However, polymorphisms do occur. e.g. Diptera.

Often, non-disjunction rates low; e.g *Mus.*

However, should still be some heterozygous disadvantage, leading to fixation. Can cause a partial barrier between populations that are fixed for different rearrangements.

Possible mechanisms: "the shifting balance"



Chromosomal evolution and speciation

Species: characterised by an absence of hybrids, by hybrid inviability, or sterility of hybrids.

Barriers between chromosome races therefore similar to barriers between specie ⇒ chromosomes important in speciation?

Controversial that chromosomal evolution CAUSES speciation on its own (MJD White, Guy Bush 1970s, "stasipatric speciation").

But chromosomal rearrangements do contribute the the isolation between species, because species often differ chromosomally.

For example, humans have a chromosome number of 2n = 46, whereas chimps have 2n = 48. Humans differ from their closest relatives by 9 pericentric inversions and one centric fusion.

> Hybrids would almost certainly be very infertile, based on chromosomal problems alone, because they would be heterozygous for so many different rearrangements.

Possible advantages to chromosomal mutants

Are there any advantages to chromosomal rearrangements? As we mentioned at the start, there may be *position effects* - *cis*-acting effects which change gene regulation.

There may also be advantages due to reductions or increases of recombination; again we know little about these.

These may also affect speciation; could allow speciation when in contact, by protecting adaptive traits. c.f. recent results in *Drosophila*.

TAKE HOME POINTS

- Positions of genes along chromosome rarely important, although "position effects" are known.
- However, chromosomes themselves have very strong holistic, selective effects. Chromosomal rearrangement heterozygotes often suffer reduced fertility, causing het. disadvantage.
- Polymorphisms rare within species; polymorphisms are usually unstable. Species may differ in karyotype, however, and often do.
- In some groups, chromosomal polymorphisms seem much more common within species.
- Chromosomal evolution may involve an initial period of genetic drift, but this is controversial.
- Because species often differ in karyotype, it is tempting to speculate that chromosomal evolution is involved in speciation, but this is controversial also.

FURTHER READING

FUTUYMA, DJ 2005. Evolution. Chapter 8 (181-185)

FUTUYMA, DJ 1998. Evolutionary Biology. Chapter 10 (pp. 286-294); for shifting balance: Chapter 14 (pp. 408-409).

For introduction to chromosome structure and function: L. HARTWELL, L. HOOD, M.L. GOLDBERG, L.M. SILVER, R.C. VERES, A. REYNOLDS (2003) Genetics: From Genes to Genomes. McGraw-Hill, chapters 12-13.