

Outline of lectures 24-26

Chromosome Evolution

1. Chromosomes can change by many kinds of rearrangement. These involve breakage of chromosomes and rejoining. Chromosomes when broken have “sticky ends” that seem to want to be healed by sticking to another sticky end. For decades this stickiness was a mystery. But we now know that these sticky ends are DNA helices, whose stickiness comes from a partially single-stranded stretch at the end. *Telomeres*, the ends of the chromosomes, are not sticky – we now know that they have a covalent bond across the end of the chromosome between the two helices.
2. *Inversions* are rearrangements that make two breaks in the same chromosome, and flip the piece in between. They are of two types: *pericentric* (inversions that include a centromere) and *paracentric* (those that do not). In parts of the U.S. these two terms are pronounced distinctly, in other parts identically.
3. Immediately after an inversion occurs, or after an inversion chromosome is passed on to an individual which also has a normal, uninverted chromosome, the individual is an *inversion heterozygote* (its chromosomes having two different gene orders – the individual genes may or may not be heterozygous). Heterozygotes for inversions form a loop at 1st division of meiosis.
4. Recall that just before meiosis, each chromosome duplicates into two *chromatids*, held together by the centromere. When two homologous chromosomes pair at metaphase of the first division of meiosis, there are then a total of 4 strands in the pair. These are later separated out into the four products of the meiosis by the first and second divisions of meiosis.
5. In heterozygotes for paracentric inversions, if there is crossing-over in such a structure, two gametes of the four are normal, one has two centromeres and forms a chromosome *bridge* and the other has no centromeres and gets lost.
6. The bridge structure is stretched between the two products of the first meiotic cell division, and it breaks at an unpredictable point on the bridge.
7. The result are gametes that have big duplications or deficiencies, so they do not have the same number of copies of all loci. This generally results in lethality (or at least sterility) of the offspring.
8. (*Not covered in lecture*). In *Drosophila*, however, there happens to be no crossing-over in males, and in females the cells line up in such a way that a bridge will involve two of the three cells out of four that will not be parents of the egg. So the loss of offspring by

crossing-over in paracentric inversions is much less in *Drosophila*. As a result they have a lot of polymorphisms for paracentric inversions.

9. Pericentric inversion heterozygotes also form a loop at meiosis. In that case, crossing-over does not lead to bridge-fragment problems, but results in two of the four gametes being duplication/deficiency gametes, and again the offspring getting them do not survive.
10. Thus inversions will generally be partially underdominant (to the extent that there is crossing-over within them) and they will be strongly selected against. A new inversion will be rare, and thus may be able to fix only in small populations, or if it happened to occur in a highly fit chromosome.
11. Once they fix, the new population is not at any disadvantage (at least unless there are “position effects” which make genes care where they are on the chromosome).
12. *Translocations* are double-break events that exchange a segment of one chromosome with part of another. In heterozygotes, a cross configuration forms at meiosis. If the segregation is *adjacent*, duplication-deficiency problems arise and the gamete will result in inviable offspring. If the segregation is *alternate* there is no such problem. The fraction of adjacent segregations is near 50% but varies depending on how close to the centromeres the break points are.
13. Crossing over modifies which kind of segregation – adjacent or alternate – gets the gamete into duplication-deficiency trouble, but it’s about 50-50 in either case.
14. Thus translocations too will have trouble spreading through a population as a result of being underdominant.
15. The preceding kinds of rearrangements change the relative sizes of chromosome arms but not the numbers of chromosomes.
16. Chromosome numbers vary widely (from 1 pair to 630 pairs!) and there is no obvious correlation of this with anything of evolutionary importance. However they do change slowly, so related species do have similar chromosome numbers.
17. Chromosomes can be *metacentric* (have two roughly equal-sized arms) *acrocentric* (have two very unequal-sized arms), or *telocentric* (have one noticeable arm and the other too small to be noticed).
18. *Robertsonian fusions or fissions* are rearrangements that combine two telocentrics into one metacentric (or one acrocentric), or which split one chromosome into two telocentrics.
19. (*Not covered in lecture but worth mentioning*). After a Robertsonian rearrangement there may be segregation problems in a chromosome heterozygote, unless the two centromeres of the telocentrics tend to go to the same pole. These problems can again result in underdominance.

20. Chromosome rearrangements can be used to infer phylogenies. This use will increase as comparative genomics becomes more intensively studied, as genetic maps (and full genetic sequences) of many species become available.
21. An interesting case where comparative genomics has already been helpful has been in the Hawaiian species of the genus *Drosophila*. Being dipterans (flies) they have giant salivary gland chromosomes which are not only polytene (multiple stranded) and can have many bands identified on them by staining for DNA, but also the two homologues are paired in this larval salivary gland! (This must be a preadaptation for the convenience of the geneticist).
22. In Hawaii there are over half the world's species of *Drosophila*, apparently an adaptive radiation after an invasion from the mainland of the New World about 40 million years ago (this is before any of the present Hawaiian islands existed – this would have been to previous islands that are now seamounts to the northwest).
23. Harrison Stalker and Hampton Carson, in the 1960s and 1970s, used the banding patterns to make a phylogeny of the 92 species of one large group, the “picture-wing” group, of Hawaiian *Drosophila*. When we consider the geographic locations as if they were states of a character, and we use parsimony to reconstruct when they changed and in which direction, their placement on the phylogeny shows invasions of a new island frequently being associated with a speciation, and a net flow from of migrations from the northwest to the southeast. This is very consistent with the geology, which has new islands arising in the southeast, so that flies are moving southeast, colonizing new islands as they appear.
24. If two species with different chromosomes cross, if they are different enough not to pair as bivalents, big segregation problems can arise owing to *aneuploidy* (unequal numbers of different chromosomes) with duplication-deficiency gametes.
25. However, if the cross doubles the chromosome complement by an unreduced division happening, then one can get all chromosomes pairing normally. This individual is a *polyploid*, specifically a *tetraploid* (and more specifically an *allotetraploid* as its tetraploidy combines two different diploid genomes).
26. Tetraploids may be relatively normal, as they have equal numbers of all genes (though twice as many of all of them). They thus have comparable dosages of all loci. But they will produce *triploid* offspring when they mate with a normal diploid, and those do not have proper segregation and get into big trouble with aneuploidy when they produce gametes themselves.
27. A tetraploid thus would be best off mating with another tetraploid, and is thus a “hopeful monster” with no one to mate with.
28. Formation of new species by tetraploidy is common among angiosperm plants that often have both sexes present on the same plant. They then have no sex chromosomes and also have at least the possibility of self-fertilizing. Animals have tetraploidy much more

rarely (there are some exceptions: most vertebrates appear to have had their genomes doubled twice in the ancestral lineage, and salmonid fishes are all doubled compared to their relatives) . This may be owing to problems with sex-determination in XXYY individuals and owing to not being able to self-fertilize.

29. There are thought to have been at least two genome doublings in the lineage from the origin of vertebrates to us.
30. Angiosperm plants often have groups that have numbers of chromosomes that are sums of smaller numbers that are also present. Thus in the herbaceous plant *Clarkia* we find species with 8 pairs of chromosomes, some with 9 pairs, some that are tetraploids with 17 pairs (= 8 + 9) and some that are hexaploids with 26 (= 17 + 9).
31. Is there anything special about our chromosome numbers or shapes? Humans have 46 chromosomes (23 pairs), some of them large metacentrics and a fair number of smaller acrocentrics. This is about average for eutherian (placental) mammals, which range from 6 (in the Indian Muntjac) to about 80.
32. Great apes have 48 chromosomes – there seems to have been a Robertsonian fusion in the lineage to humans, who have 46 chromosomes. Which chromosomes fused is known. The result is human chromosome 2, a large metacentric. There is no reason to believe that this fusion was a particularly important event in the evolution of humans – it is just something that happened at that time.
33. Distributions of numbers of chromosomes and of their shapes (arm ratios) in various groups seem to come close to those predicted by random rearrangement models (computer simulation work by H. Imai, T. Maruyama and Ross Crozier).
34. For a more comprehensive argument that many features of genome evolution are the result of random changes (rather than natural selection optimizing the numbers and lengths of chromosomes, or the order of genes), see Michael Lynch's recent book *The Origins of Genome Architecture*.
35. The number of chromosomes in eukaryotes ranges from 2 (the Australian ant *Myrmecia* – males are haploid, and so have one chromosome) to about 1260 (the fern *Ophioglossum reticulatum*). The latter is probably the result of multiple rounds of polyploidy. With too many chromosomes, there are likely to be segregation problems. While this keeps the numbers from going too high, within that constraint it is a good “null hypothesis” that the karyotype (the chromosome numbers and shapes) evolves randomly and that there is little or no selection for it to have a particular form in particular species.
36. Amounts of DNA are not, contrary to one's naive expectation, correlated closely with the complexity of the organism. The Congo Eel (*Amphiuma*) a particularly nasty legless salamander, is the DNA champion among tetrapods with 26 times as much DNA per cell as humans. The lungfish *Lepidosiren* is the champion among vertebrates with about 40 times as much as humans. It is believed that this is the mostly result of having a lot of junk DNA.

37. Recently (in 2012) the ENCODE Consortium (ENCyclopedia Of DNA Elements) reported finding many transcription factor binding sites in areas of the human genome far from genes. Together with evidence that there is RNA transcription from most parts of the human genome, this led them to make the dramatic announcement that the idea that there was lots of “junk DNA” in the human genome was now dead, that most of the genome had “function”.
38. That was the main conclusion that the science press reported, and it was a sensation. This was understandable given what the ENCODE paper and press conference said.
39. However, many molecular evolutionists are skeptical of that conclusion. They point to four major lines of evidence supporting the idea of junk DNA:
 - (a) Genome sizes vary greatly among organisms that have comparable complexity (the Onion Test – is it true that onions more complex than us?)
 - (b) Most regions of the genome are not conserved by natural selection.
 - (c) Large genomes would confer too high a loss of fitness by mutation (the Mutational Load).
 - (d) Large fractions of the genome are readily annotatable families of transposons and other selfishly-replicating elements.
40. The ENCODE consortium has since 2012, under a barrage of criticism from molecular evolutionists, backed away from their statements about junk DNA being disproven. But they have backed away *very very quietly*, which is irresponsible.
41. Popular science audiences, including other kinds of scientists, have not gotten the word and many people may think that it has been shown that there is no junk DNA. In short, the broader perception of the issue has been set back 10 years, and we are still trying to recover from that.
42. The one thing that is sure is that when popular science reporters say that genomicists used to think that all noncoding DNA was junk, they are showing their ignorance. No one ever thought that.
43. Comparative genomics is resulting in rapid increase of knowledge about human inversion polymorphisms (a number of these have been found) and also the number of inversions in the lineages separating human and chimp. A recent study using the human and chimp genome sequences found 1576 inversion differences between the species, almost all not big enough to include the centromere. Only 29 of the inversions had a breakpoint in a gene. More than 1500 of them were less than 15 kilobases long.
44. The genes on different chromosomes in humans can be located in other completely sequenced genomes. There are almost no changes of chromosome location between humans and chimps, except for the fusion of two chimp chromosomes to be the human 2nd chromosome. Between human and mouse there are quite a few major rearrangements (100-200 of them) of blocks.