Business

- Helpful video on translocations:
  https://www.youtube.com/watch?v=WqHEndYJEkQ
- Homework due WEDNESDAY because of holiday
- Practice problems (including last year's exam) on web site

Selfish DNA

- How can a gene be "selfish"?
- Kinds of selfish DNA
  - Meiotic drive (previously discussed)
  - Repeats
  - Transposons

Selfish DNA

- Regular genes:
  - Replicate only when genome replicates
  - Increase their fitness by increasing organism's fitness
  - "Motivated" to work well with the rest of the genome
- Selfish genes (or genome regions):
  - Replicate independently, or otherwise control their own reproduction (t chromosome)
  - Can increase their fitness without increasing organism's fitness, by making more copies of themselves
  - Gene's fitness is less dependent on working well with the rest of the genome

Examples of potentially selfish DNA

- Repetitive elements (microsatellites, etc)
- Transposons
- Meiotic drive loci (t chromosome)

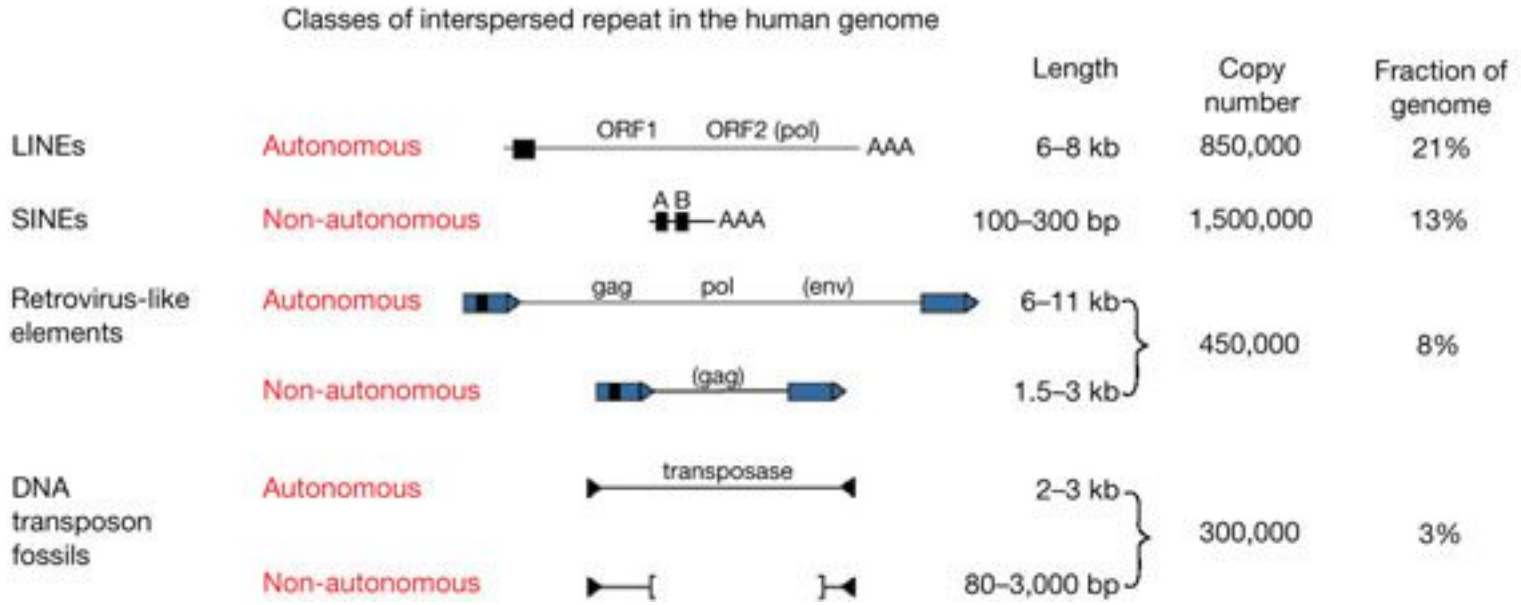
How does repeated DNA increase?

- Hard to duplicate repeats accurately:
  - Replication slippage (same area gets replicated twice)
  - Unequal crossing over
- Genetic drift can then cause copy number to increase or decrease
- Microsatellite rate of copy number change up to 10^{-4} per meiosis (compare single-base mutation rate 10^{-9})

How does repeated DNA increase?

- Number of repeats cannot decrease below 1 by these mechanisms
- Mathematically, a random walk with a barrier in only one direction will tend to move away from the barrier
- This might be kept in check by selection against the repeat:
  - DNA replication is expensive
  - Cells with lots of DNA divide slower and are larger
  - One repeat more or less makes little difference!

Consequences of a transposition



- Inactivate or truncate a gene
- Detach a gene from its promoter
- Put gene under control of the transposon promoter

Mobile elements

- Conservative transposition:
  - transposable element leaves its original position and moves to a new position
  - because of chromosome reassortment, can increase or decrease genomic copy number
  - can also increase copy number if transposition happens during DNA replication (transposon replicates, moves, and replicates again)
  - causes mutations which may cleanly revert when transposon leaves
  - often a small duplication is left at the site

- Typical of most DNA transposons

Mobile elements

- Replicative transposition:
  - transposon stays where it is; a new copy inserts elsewhere
  - increases copy number
  - causes mutations which do not easily revert
  - this can happen via DNA copying or via DNA to RNA reverse transcription
  - also tends to cause a small duplication at the site

- RNA transposons (retrotransposons) and some DNA transposons

Heavy spotting shows activity of Mu transposon

Are retrotransposons viruses?

Two hypotheses:

- RNA virus from a retrotransposon:
  - Cell evolved reverse transcriptase for its own use
  - Transposon picked up a protein that could form a virus capsule and became a virus
- Retrotransposon from an RNA virus:
  - Virus infected cell and then lost ability to leave
  - Reverse transcriptase now allows it to move within the cell
- Both of these may have happened at different times to different viruses/transposons!

A Drosophila mystery–hybrid dysgenesis

- Lab strains were isolated from the wild about 100 years ago
- When lab female x wild male, F1 hybrids show:
  - Low fertility (F1)
  - Birth defects (F2)
  - High mutation load (F2)
  - Chromosomal rearrangements (F2)
- Lab male x wild female cross does not show dysgenesis

Drosophilia P element

- Present in wild flies only
- No transposition in somatic cells
- In wild flies:
  - Suppressor in cytoplasm prevents transposition
- In wild male x lab female:
  - High transposition in germ line cells
  - Hybrid dysgenesis

• *P*-element structure

Figure 14-16

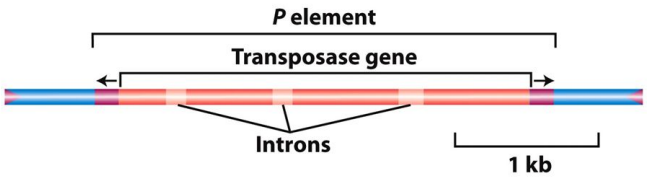


Figure 14-16
Introduction to Genetic Analysis, Ninth Edition

Two theories about P

1. Wild strains all gained P since the lab strains were collected
   - $D.\ melanogaster$ is globally distributed
   - Would require a world-wide sweep of P
2. Lab strains used to have P but lost it
   - Separate lab strains evolved in isolation
   - Maybe something about lab life removes P?

Is P element a new invader?

- Current evidence is that P is new in wild strains
- Very similar P found in a distant relative (60 million years' separation)
- Lab strains do not have:
  - Broken copies of P
  - Supressors needed to restrain P
- P may have come in via rare cross-species mating
- It spreads because it can move around in the genome

Transposition: good or bad?

- If P truly spread across the world in 100-200 years, it's clearly good–for the transposon
- P moving in somatic cells kills the flies
- P moving at a high rate in germ cells is pretty bad too
- P-bearing strains experience strong selection for silencing of P
- P element can fight back by evolving immunity

Evolutionary effects of transposons–discussion

- What would be different between a species with transposons and a similar one without?

- Consider effects of:
  - Mutations
  - Similarity between different parts of the genome
  - Genome size

Thought problem

- Cross P into a lab strain and maintain a population in bottles
- Experimentally, population may live or die
- Which is likely to do better, a large or small population?

Thought problem

- Cross P into a lab strain and maintain a population in bottles
- Experimentally, population may live or die
- Which is likely to do better, a large or small population?
- When this experiment has been done, large populations are more likely to survive

Transposons in bdelloid rotifers

- Five species of bdelloids lacked major retrotransposon families (Tc1, LINE, Gypsy)
- All other tested phyla had at least one of these, usually all three
- Bdelloids *did* have Mariner-type transposons (DNA transposon)
  - These can be transmitted horizontally
- "Retrotransposons are sexually transmitted nuclear parasites" – Arkhipova and Meselson 2000

Horizontal transfer

- Obtaining a gene from a different species or lineage:
  - Cross-species hybridization
  - Viral transformation (virus carries in a gene)
  - Gaining genes from an endosymbiont
    - *Plasmodium vivax* appears to contain significant human DNA
  - Picking up DNA from the environment
- About 8% of bdelloid genome is bacterial in origin

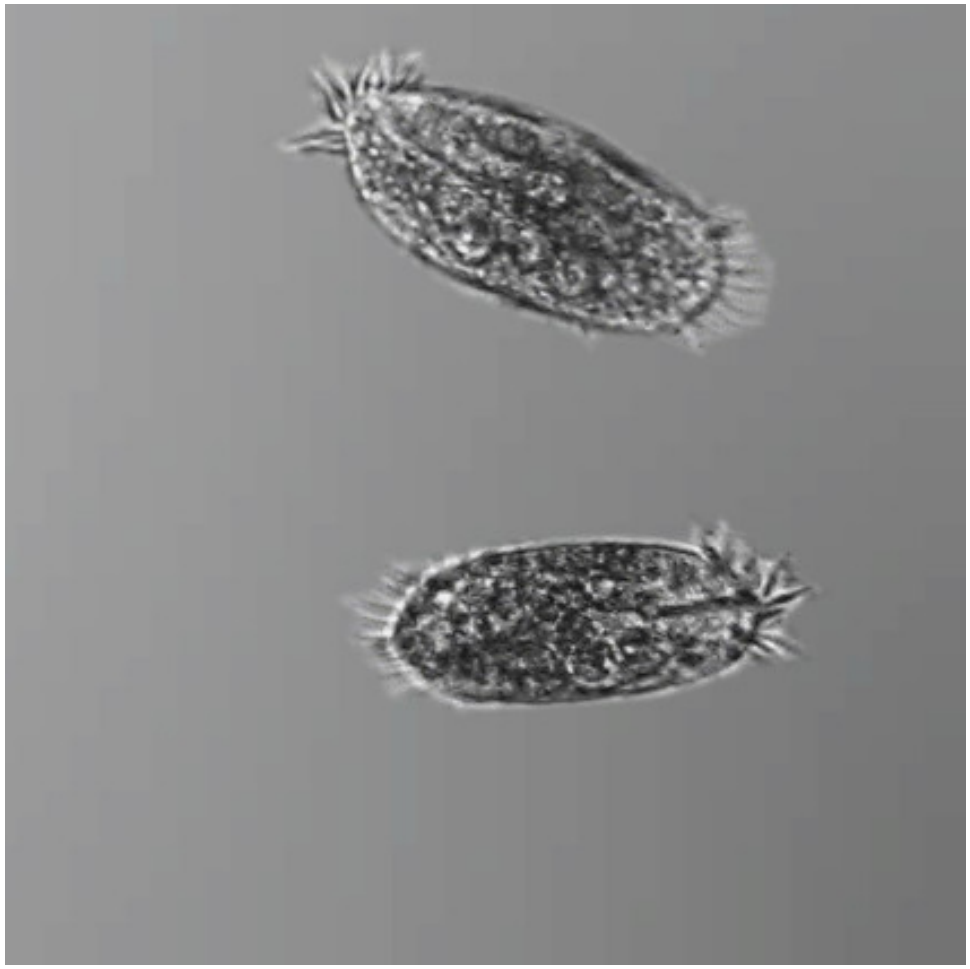
McClintock's "genome shock" hypothesis

- Transposons could allow an organism to control its mutation rate:
  - Suppress transposition when well adapted
  - Permit transposition when struggling, "hoping" for a useful mutation
- Alternative hypothesis: transposons are purely selfish
  - Suppress transposition whenever possible
  - Fail to suppress transposition when badly stressed
- Not easy to test these alternatives

One supportive observation

- *Copia* transposons in flies carry a heat-shock promoter
- Transposition is triggered when flies are stressed
- Hard to distinguish between:
  - Heat-shock regulation of transposons helps the fly
  - Heat-shock regulation of transposons helps the transposon

Finding a use for transposons

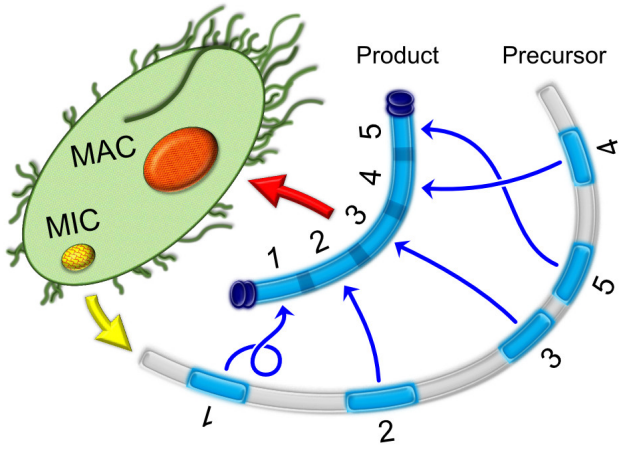


Oxytricha genome rearrangement

- Two nuclei per cell:
  - Micronucleus used for reproduction, but genes not active
  - Macronucleus expresses genes
- Macronucleus genome is highly rearranged:
  - Cut into around 16,000 tiny chromosomes
  - Usually 1 gene per chromosome
  - Genes are re-assembled from fragments
  - Some are duplicated (dosage control?)
  - 95% of germline genome is destroyed

Transposons harnessed to chew up genome

- Germline genome of *Oxytricha* full of transposons
- Macronucleus has none
- If transposases are inactivated, the macronucleus fails to develop properly
- Transposons and transposase probably central in rearrangement process



Other "tamed" genome rearrangements

- Vertebrate rearrangement of antibody genes
  - Genome contains assortment of V, D and J segments
  - Targeted rearrangement makes a final antibody gene
  - This system greatly increases antibody diversity
- Yeast sex switching
  - Genome contains inactive copies of a and α genes
  - Targeted gene conversion allows sex switching
- Evolution can "use" elements which were initially selfish

One-minute responses

- Tear off a half-sheet of paper
- Write one line about the lecture:
  - Was anything unclear?
  - Did anything work particularly well?
  - What could be better?
- Leave at the back on your way out