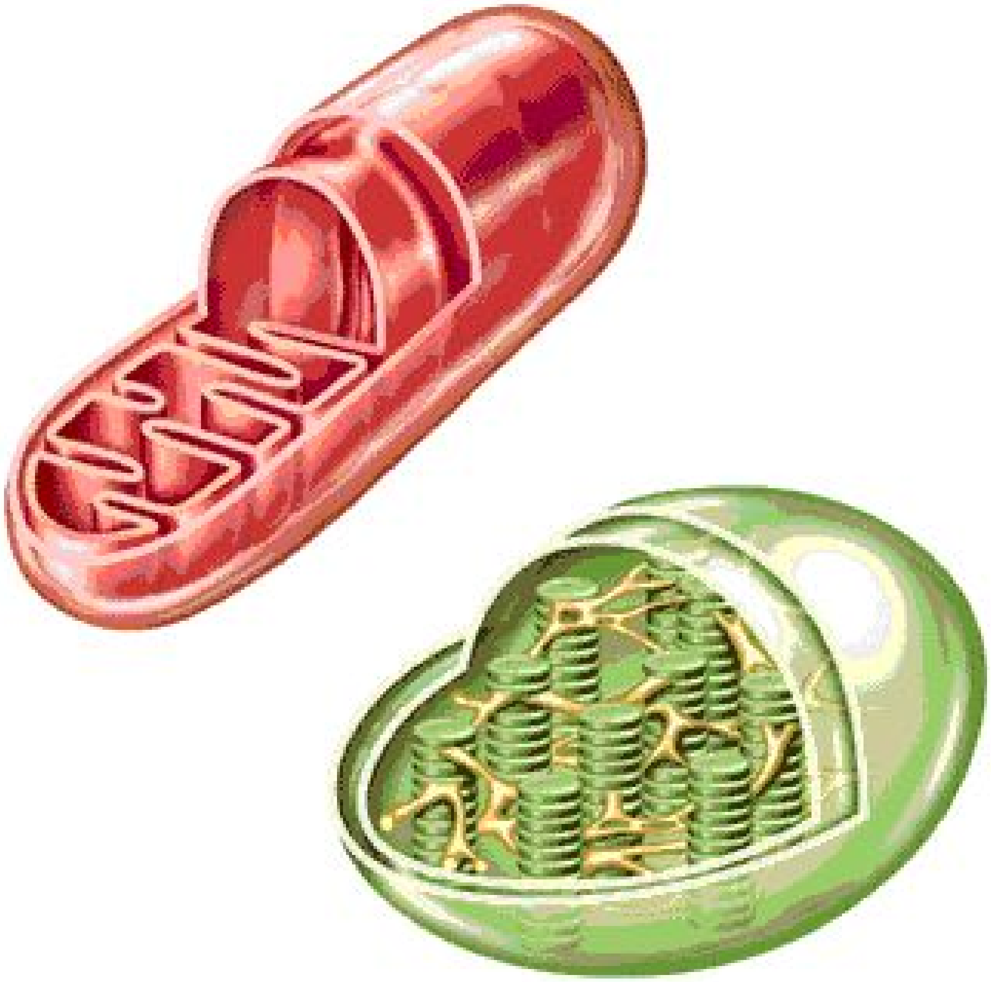
Roadmap

- History of viruses
- Competition among levels of organization
  - Mitochondria versus host cell
  - Wolbachia versus host organisms
  - Multicellularity and eusociality

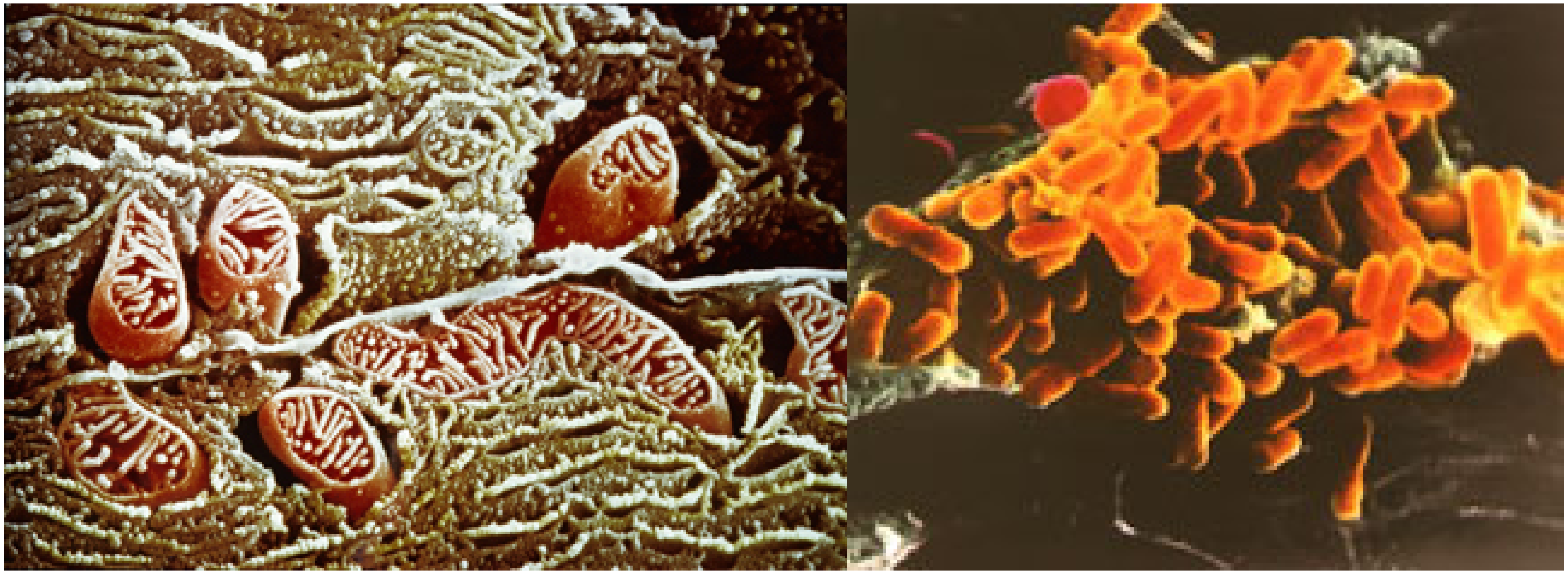
One-minute responses

- Q: I thought viruses arose first, then prokaryotes and eukaryotes–?
- A: Since viruses need other organisms to replicate, they can't have come first
- Viruses probably aren't even a group:
  - Nothing in common among DNA and RNA viruses
  - New virus can arise from a transposon at any time

Self-replicating organelles



Mitochondrion

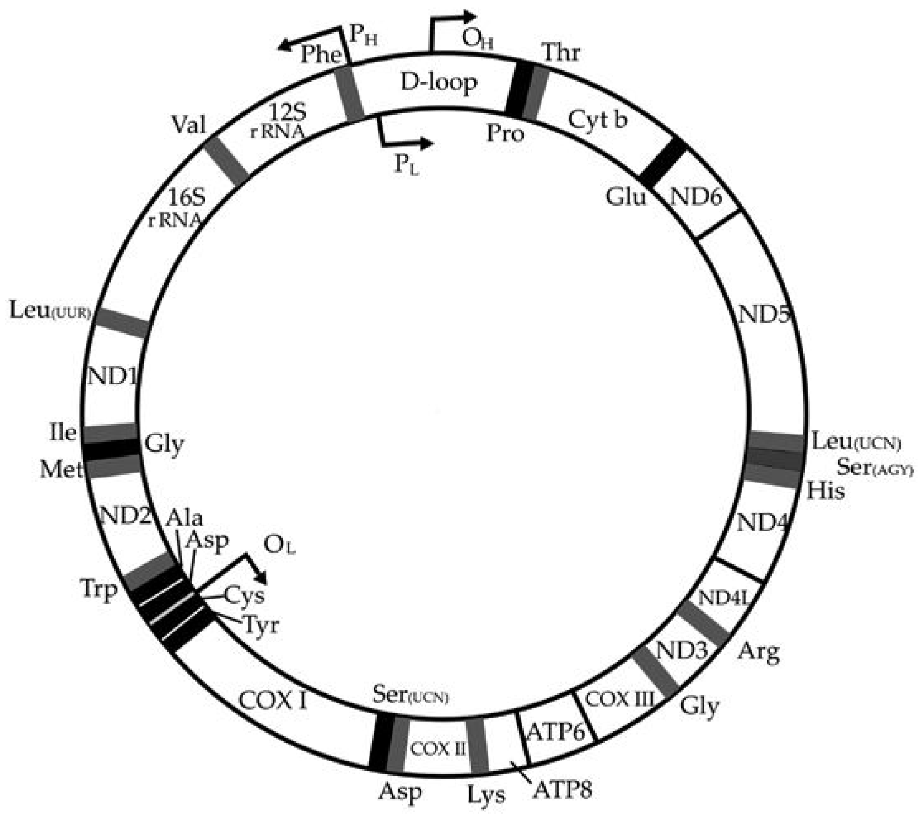


- Most likely relative is a procaryote related to Rickettsia
- Human mtDNA genome contains 37 genes, whereas smallest known bacterium contains 521
- Genome has shrunk dramatically since "capture"

Why do we think mitochondria are captured bacteria?

- Circular genome
- Variant genetic code, shared with proteobacteria:
  - UGA means tryptophan instead of "stop"
  - AUA means methionine instead of isoleucine
- Ribosome size is 70S (bacterial) not 80S (eukaryotic)
- Genes group with prokaryotic genes in a phylogeny, not eukaryotic genes (with some exceptions)

Mitochondrion



What makes mtDNA so interesting for molecular evolution studies

- High mutation rate due to poor repair (in animals, but not in plants)
- Haploid (generally no recombination)
- Maternal transmission (in vertebrates)
- Abundant in cells so easy to purify from fossil or forensic material
- Flow of genes between nuclear and mitochondrial genome

Competition between mtDNA and nucleus

- Yeast "petite" or $\rho-$ mutation
  - Colonies grow very slowly
  - Mitochondrial genome reduced to multiple copies of the origin of replication
  - This out-competes normal mitochondria

- Such problems are probably common in other eukaryotes, but are lethal so not observed

Competition between mtDNA and nucleus

- Mutations like $\rho-$ are bad for the organism
- Competition among mitochondria for better fitness reduces organismal fitness
- Over evolutionary time, genes move from mtDNA to nuclear DNA
- Reverse transcription? Transposition? Salvage from dead mitochondria?
- Reduces potential selection on mtDNA

mtDNA practice problem

- If the effective population size of a nuclear gene is 2N, what is the effective population size of mtDNA?

- It may help to know that the egg normally contributes only one lineage of mtDNA to the embryo

mtDNA practice problem

- If the effective population size of a nuclear gene is 2N, what is the effective population size of mtDNA?

- Lose a factor of 2 because mtDNA is haploid

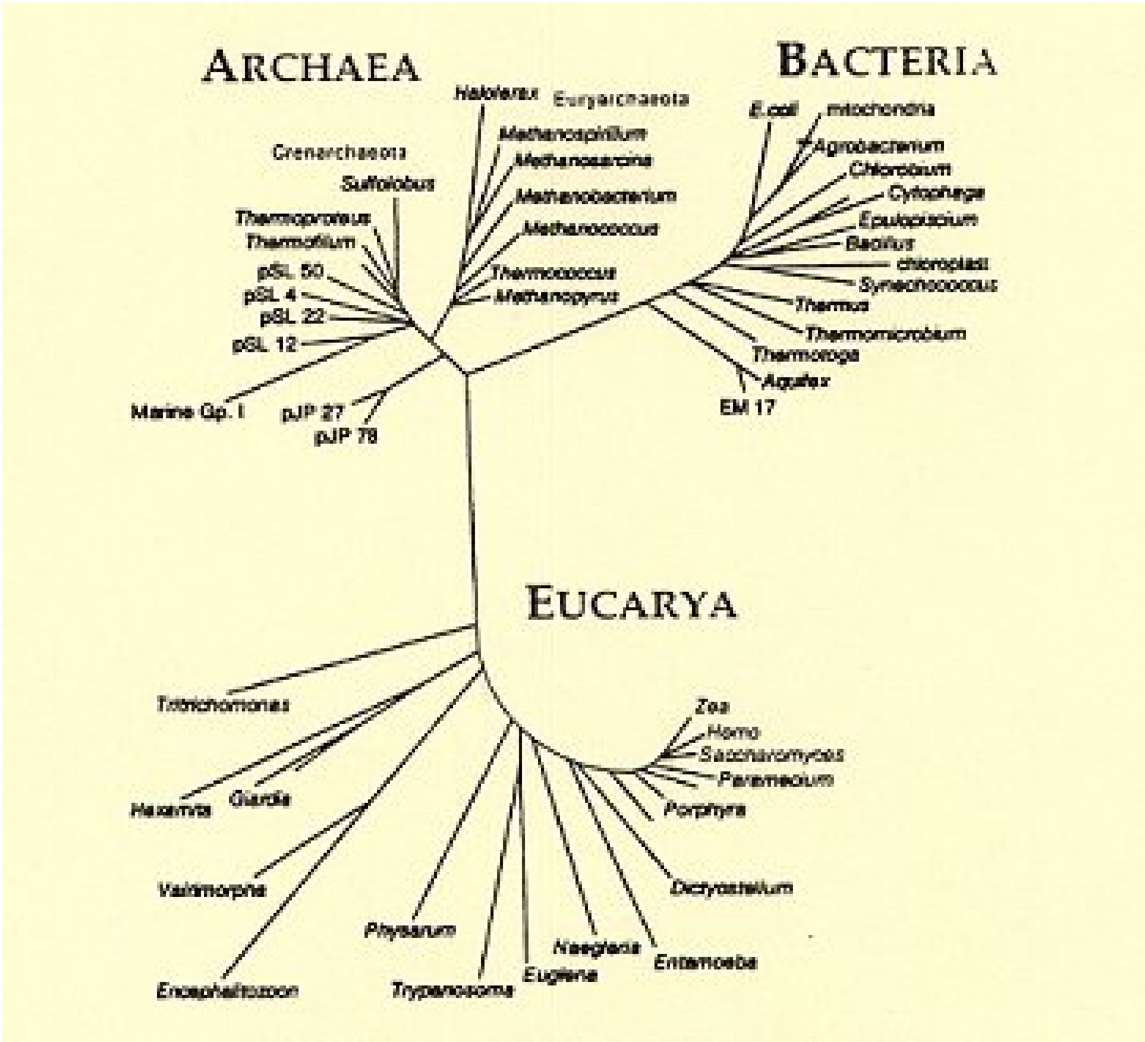
- Lose a factor of 2 because males don't transmit

- Drift is therefore 4 times more powerful in mtDNA than in nucleus

Giardia

- Clearly a eukaryote (it has a nucleus)
- No mitochondria and a small genome (around 5000 genes)
- Near base of eukaryotic tree of descent
- Did it ever have mitochrondria?

Giardia lamblia AKA beaver fever

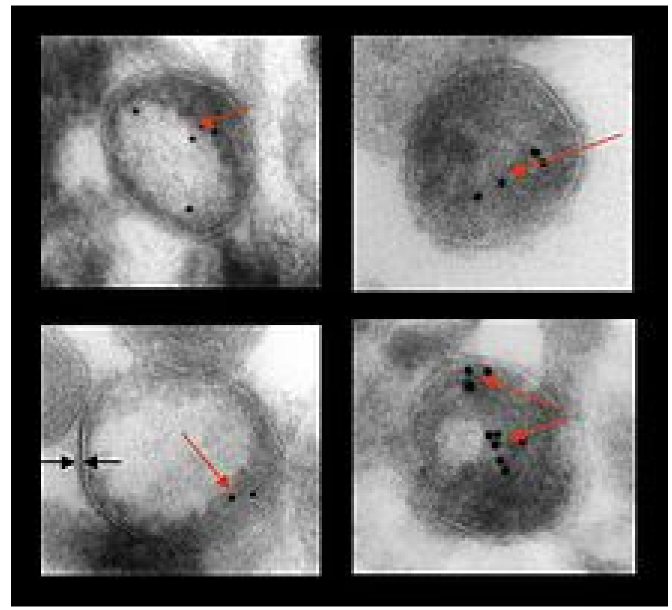

ARCHAEA
BACTERIA
EUCARYA
Euryarchaeota
Crenarchaeota
Haloferax
Methanospirillum
Methanosarcina
Methanobacterium
Methanococcus
Thermococcus
Methanopyrus
Sulfolobus
Thermoproteus
Thermofilum
pSL 50
pSL 4
pSL 22
pSL 12
Marine Gp. I
pJP 27
pJP 78
E.coli
mitochondria
Agrobacterium
Chlorobium
Cytophaga
Epulopiscium
Bacillus
chloroplast
Synechococcus
Thermus
Thermomicrobium
Thermotoga
Aquifex
EM 17
Trichomonas
Hexamita
Giardia
Vairimorpha
Encephalitozoon
Physarum
Trypanosoma
Euglena
Naegleria
Entamoeba
Dictyostelium
Porphyra
Paramecium
Saccharomyces
Homo
Zea

Giardia

- mtDNA genes are most closely related to bacteria
- Native host genes should be related to other eukaroytes
- *Giardia* has several nuclear genes involved in metabolism that cluster with bacterial genes
- Hypothesis:
  - *Giardia* originally had mitochondria
  - Genes were transferred to the nuclear genome
  - Eventually the mitochondria were not needed and were lost

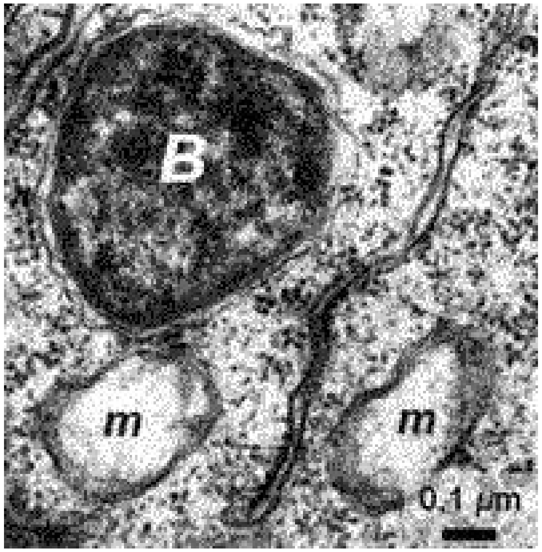
Really no mitochondria?

- *Giardia* has mitosomes:
  - Share many proteins with mitochondria
  - Involved in iron/sulfur biochemistry (like mitochondria) but do not carry out aerobic respiration
  - No genome–all genes encoded by nuclear genome



Wolbachia

- Gram-negative bacteria that live inside cells
- Infect insects, nematodes, mites and spiders
- 20%-75% of insects are thought to be infected
- Transmission mainly from mother to offspring
- *Wolbachia* has a variety of strategies to increase its own propagation



Wolbachia

- *Wolbachia* is transmitted from mother to offspring
- It “prefers” to be in a female
- In mosquitoes, it overrides the sex determining switch and converts offspring into females
- Natural selection on the hosts tries to push sex ratio back to $50/50$
- If *Wolbachia* ever wins, it will lose

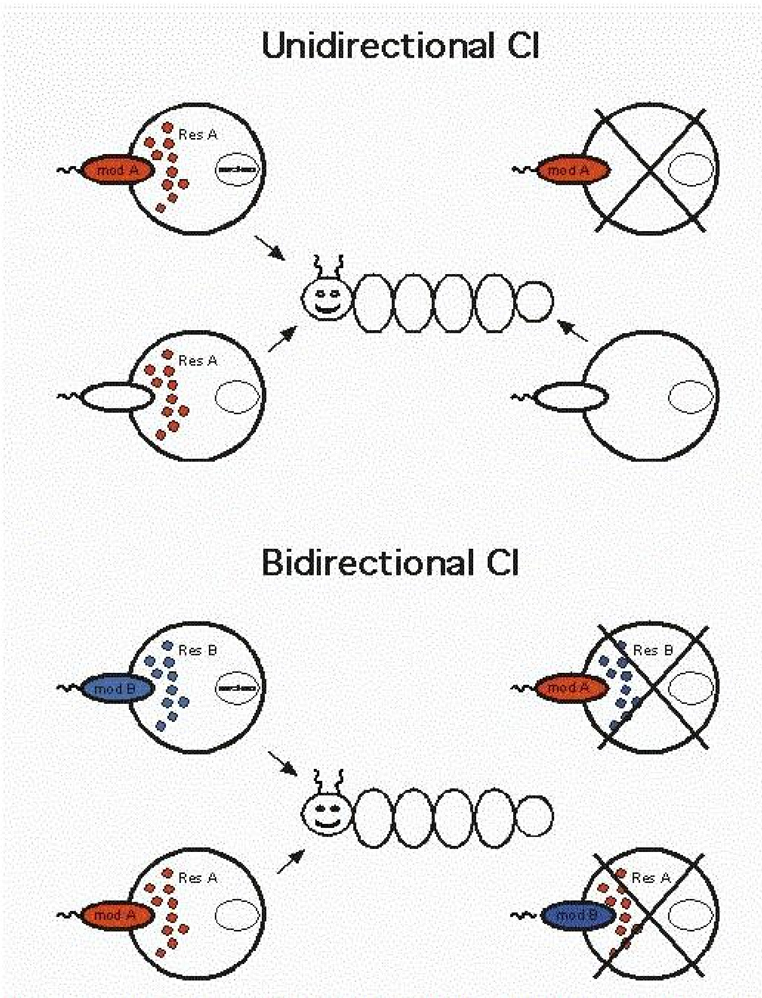
Wolbachia

- In other insect taxa, *Wolbachia* has a variety of strategies:
  - cause parthenogenesis (females clone or self-fertilize)
  - kill males
  - favor fertilization by female-producing sperm over male-producing sperm (within an infected female)
  - cytoplasmic incompatibility

- All of these strategies enhance mother-to-offspring transmission

Cytoplasmic incompatibility

- Unidirectional incompatibility: sperm modified by $Wolbachia$ can't fertilize uninfected eggs
- Bidirectional incompatibility: sperm with different strains of $Wolbachia$ can't fertilize eggs infected by each other
- Both strategies increase the proportion of $Wolbachia$-infected hosts in the population
- (Remember that sperm may contain $Wolbachia$ proteins but they can't transmit $Wolbachia$; only eggs can do that)


Unidirectional CI
Res A
mod A
mod A
Res A
Bidirectional CI
Res B
mod B
Res B
mod A
Res A
mod A
Res A
mod B

Practice problem

- Consider the following population:
  - 50% of both sexes are infected with *Wolbachia*
  - Sperm from an infected male cannot fertilize a healthy female (CI)
  - The insects do not know this and mate at random (and just once each)
  - Population size remains constant
- What proportion of insects in the next generation is infected?
- Is this better than *Wolbachia* would do without the CI?

Practice problem

With CI	Infected males 0.5	Normal males 0.5
Infected females 0.5	0.25 Infected	0.25 Infected
Normal females 0.5	0.25 Dead	0.25 Normal

0.67 Infected, 0.33 Normal

Without CI	Infected males 0.5	Normal males 0.5
Infected females 0.5	0.25 Infected	0.25 Infected
Normal females 0.5	0.25 Normal	0.25 Normal

0.5 Infected, 0.5 Normal

Wolbachia does better by killing some of the normal offspring, but this reduces the fitness of the insect population

Wolbachia and speciation

- Bidirectional incompatibility could lead to “instant speciation”
- Populations infected by different strains of *Wolbachia* are reproductively isolated
- These “species” can be fused into one by antibiotic treatment!
- Naturally occuring antibiotics probably explain why not all insects have *Wolbachia*

Wolbachia and speciation

A study that should be done:

- Do insect groups with *Wolbachia* form new species more rapidly than those without?
- Once *Wolbachia* prevents fertile mating, there is evolutionary incentive to evolve pre-mating isolation
- Eventually *Wolbachia*-separated groups may turn into true species

A medical mystery

- The disease river blindness (onchocerciasis) is caused by parasitic nematodes (worms)
- Treatment with doxycycline improves prognosis
- Doxycycline is an anti-bacterial antibiotic that does not kill worms
- Why does it help?

A medical mystery

- The nematodes are infected with *Wolbachia*
- Two factors:
  - Eye damage is driven by *Wolbachia* proteins
  - Nematodes cured of *Wolbachia* fail to develop normally
- The host has become dependent on its parasite

A thought about mitochondria

- The mitochondrion is often described as a bacterium "enslaved" by a eukaryotic cell
- *Wolbachia* suggests that the initial relationship could have been parasitic
- The small mitochondrial genome could represent nuclear self-defense:
  - *Wolbachia*'s tricks tend to reduce host fitness
  - Hosts which "tame" *Wolbachia* will have an advantage
  - Moving genes out of the mitochondrial genome might reduce its opportunities to cause trouble
- Same story could happen with chloroplasts

Evolutionary conflicts

Potential conflict whenever:

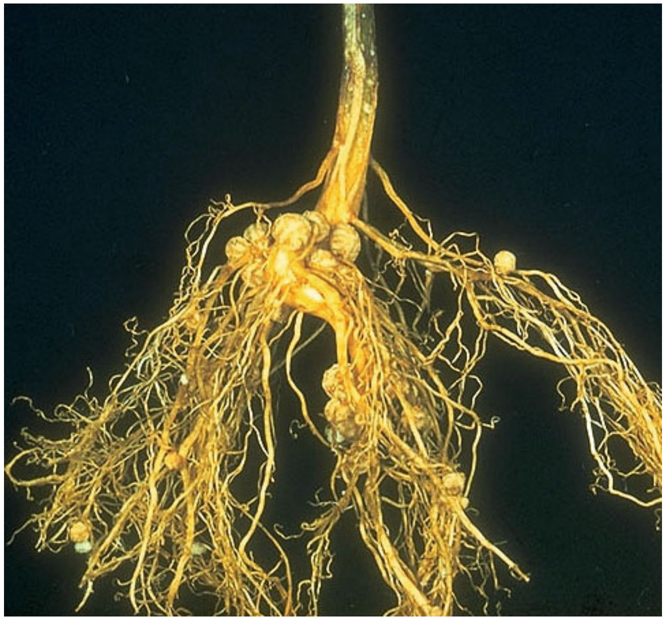
- One aspect of the genome can propagate independently of another
  - Mitochondrial replication
  - *Wolbachia*
  - Transposons
  - Cancer cells
  - Cheating worker bees
- Selection can therefore act on the individual as well as the team

Suppression mechanisms

- Reduction of organelle genomes
- Suppression of egg/sperm gene expression
- Modifier loci (for example, to block $Wolbachia$ sex-ratio distortion)
- Immune surveillance
  - HLA loci guide killing of cells expressing abnormal proteins (cancer)
  - Worker bees destroy each others' eggs

Rhizobium bacteria fix nitrogen for legumes

- Fixing excess N_2 is costly for the bacterium
- The plant needs to prevent "cheaters":
  - Nodules which don't produce N_2 atrophy
  - Plant may cut off their O_2 supply
- Such enforcement may happen within organisms as well



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