Roadmap

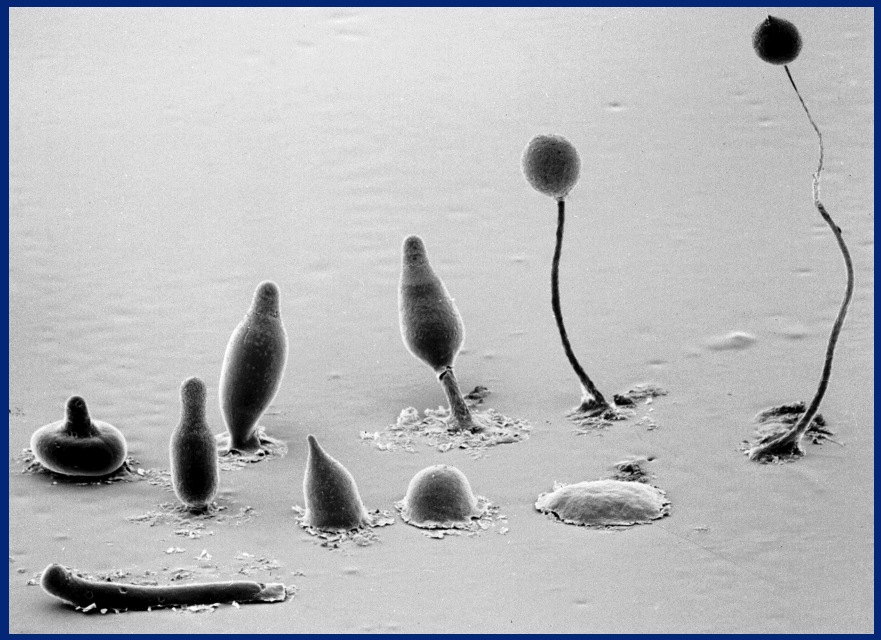
- Final exam reminder
- Competition among levels of organization:
  - *Dictystelium*
  - Devil facial tumor disease
  - *Wolbachia*

Final exam

- Mainly on second half of the course but builds on first half
- Equation sheet (similar to midterm) up on web site
- 2 hour exam but intended not to be much longer than midterm
- Time options:
  - Tuesday 3/19 at 10:30 am-12:30 pm
  - Wednesday 3/20 at 2:30 pm-4:30 pm
- If you want the graded exam back, check box on exam (otherwise I will not write detailed notes)

Group selection without kin selection

- *Dictyostelium discoides* may be an example
- Free-living amoeba band together to form fruiting bodies
- There is no apparent preference to band with kin



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The "greenbeard" effect

- Richard Dawkins coined the name "greenbeard" for a gene that can:
  - Produce a distinctive phenotype
  - Allow its possessor to recognize that phenotype
  - Cause its possessor to behave altruistically toward those who share the phenotype

- Such a gene could spread in a population

csA greenbeard gene in *Dictyostelium*

- $csA+$ individuals adhere better
- They tend to altruistically end up in the stem, not the fruiting body
- However, they recognize each other and drag each other into the slug!
- A slug from a 50/50 mix of $csA+$ and $csA-$ will produce spores that are 82% $csA+$
- The $csA-$ cells preferentially end up in the fruiting body, but only if they can get into the slug in the first place

Queller, DC, Ponte E, Bozzaro S, Strassmann SE. Science 299(5603):105-106.

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

Cancer is an evolutionary conflict

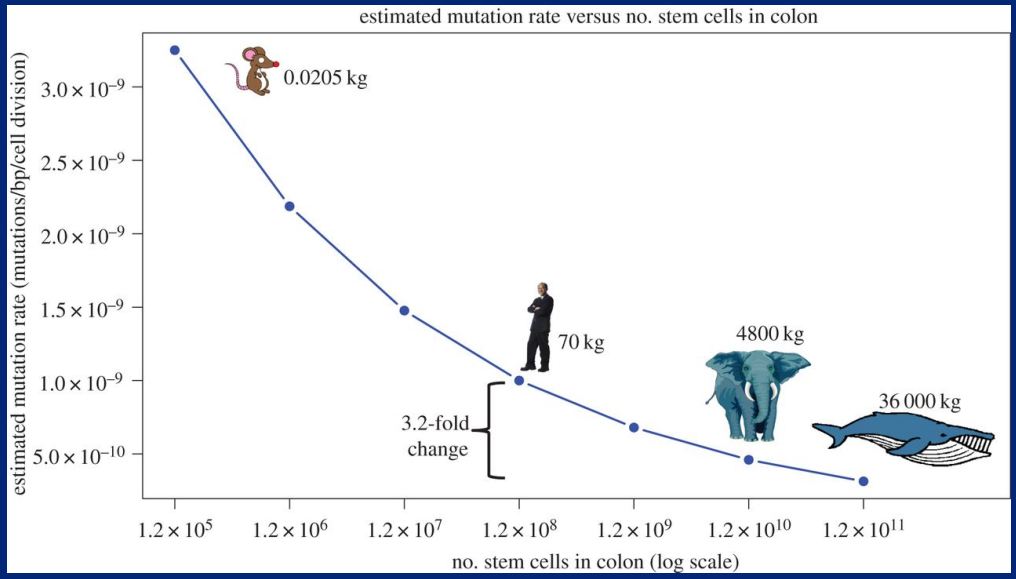
- Cell:
  - Fitness depends on individual survival and reproduction
  - Selection for faster reproduction (mutants that do this increase locally)
- Multi-cellular organism:
  - Fitness depends on management of somatic cells
  - Mechanisms like apoptosis, senescence (telomeres?), terminal differentiation
- Cancer represents victory of cell-level selection over organismal selection
- A rap song that brilliantly depicts this: https://music.bababrinkman.com/track/revenge-of-the-somatic-2

Peto's Paradox

- Mutations accumulate with number of cells and time
- This predicts that the larger and older an organism, the more cancer it should have
- Prediction is false:
  - Humans have more cancers than whales
  - In general cancer frequency does not scale with size or lifespan in mammals
- Why don't whales all get cancer? (10^{17} cells compared with 10^{9} in mice)

Peto's Paradox – ideas

- More tumor suppressors? (Elephants have 20+ copies of $TP53$)
- Better tumor suppressors?
- Lower metabolic rate?
- Tumor must be bigger to endanger life, so more time to stop it?



Ultimate cancer evolution

Tasmanian Devil Facial Tumor Disease (DFTD)

- First detected in 1996
- 70% decrease in wild population
- Transmitted by biting, especially during sex
- Next slide is an unpleasant picture–feel free to look away

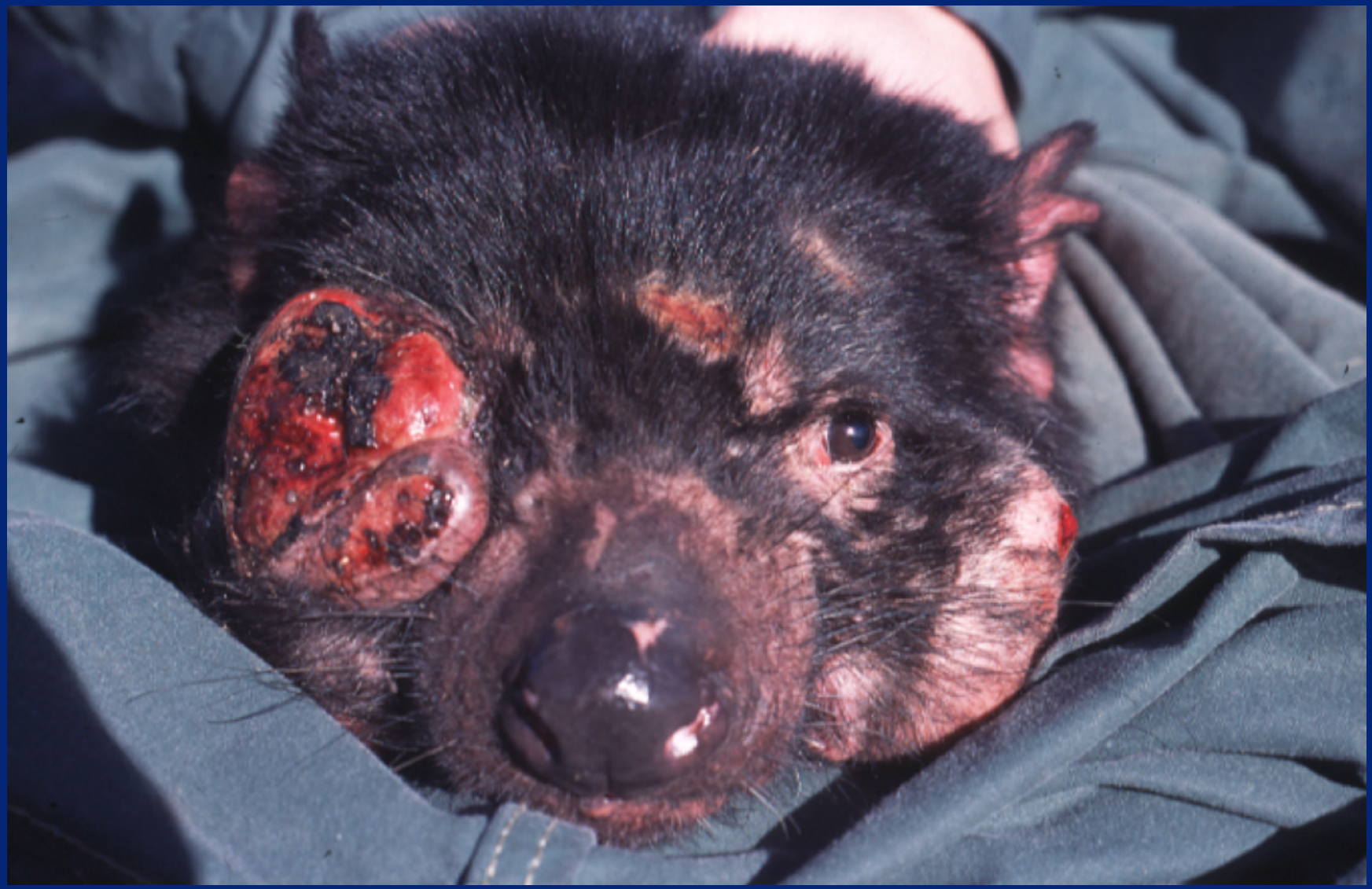


Photo: Menna Jones, from McCallum and Jones (2006) PLoS Biol

DFTD origins

- Initially attributed to an oncovirus
- DNA sequencing of animals and tumors:
  - Tumors more similar to each other than to their hosts
  - Single recent origin of tumor DNA
- Conclusion: *the cancer itself is contageous*

Evolution in action

- Host (Tasmanian devil) evolution
  - Females breed at younger age
- Parasite (DFTD) evolution
  - Evolution of multiple strains
  - Increase in tetraploid tumors which grow more slowly
  - Slow growth helps evade human projects to remove affected animals

Canine transmissible venereal tumor

- Worldwide distribution in domestic dogs
- Transmitted sexually
- Evolutionary history:
  - Based on microsatellites, diverged from canids >6000 years ago
  - Common ancestor only a few hundred years ago (severe bottleneck)
- May be becoming less virulent over time
- Other examples in hamsters and clams

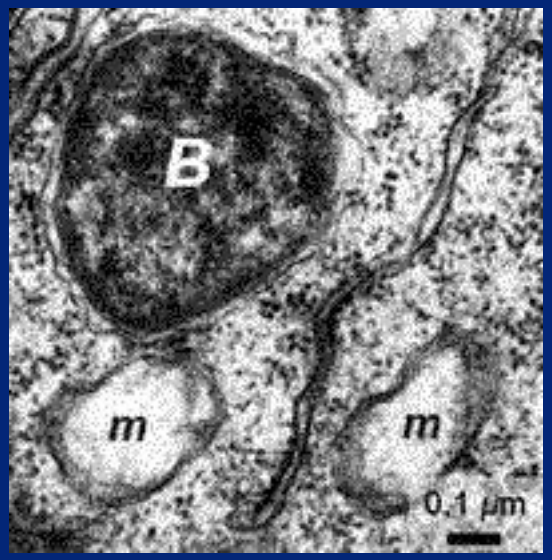
Why aren't such diseases more common?

- Multicellular organism poor starting material for single-celled parasite?
- Asexual, non-recombining lifestyle evolutionary dead end?
- Needs a vulnerable host species?
  - Devils, hamsters, domestic dogs all went through bottlenecks
- Could be more examples we haven't detected

Wolbachia

- Gram-negative bacteria that live inside cells
- Infect insects, nematodes, mites and spiders
- 20%-75% of insects are thought to be infected
- Transmission almost solely from mother to offspring

- *Wolbachia* has a variety of strategies to increase its own propagation

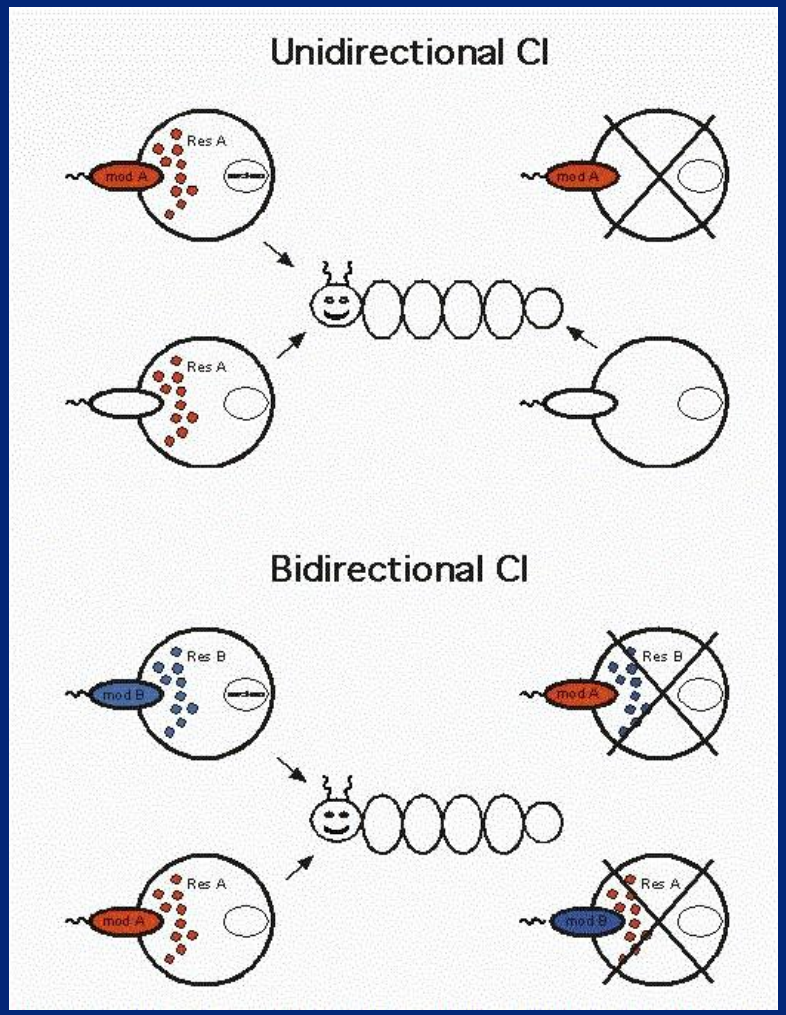


Wolbachia

- *Wolbachia* is transmitted from mother to offspring
- It "prefers" to be in a female
- Different approaches in different taxa:
  - Override the sex determining switch to convert offspring into females
  - Induce parthenogenesis (females clone or self-fertilize)
  - Decrease fertilization rate of male-producing sperm
  - Cytoplasmic incompatibility (next slide)
- All of these enhance *Wolbachia* transmission, generally at the host's expense

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*

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 caused partly by *Wolbachia* proteins
  - Nematodes cured of *Wolbachia* fail to develop normally
- The host has become dependent on its parasite

A thought about mitochondria

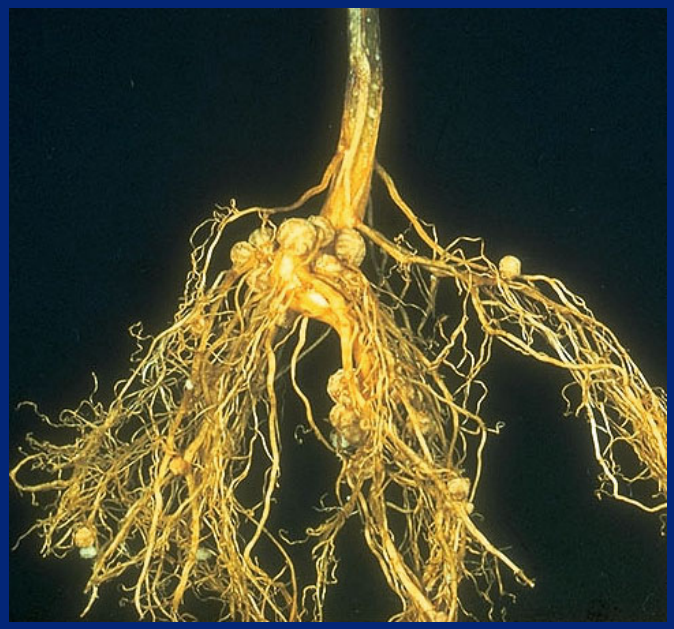
- The mitochondrion is often described as a bacterium "enslaved" by a eukaryotic cell
- *Wolbachia* suggests that the initial relationship could have been parasitic
- The small mitochondrial genome could represent nuclear self-defense:
  - *Wolbachia*'s tricks tend to reduce host fitness
  - Hosts which "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

Suppression mechanisms

- Reduction of organelle genomes
- Suppression of egg/sperm gene expression
- Modifier loci (for example, to block *Wolbachia* sex-ratio distortion)
- Apoptosis pathways
- 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



Three takeaways from this class

- Many diverse and bizarre aspects of life can be traced to simple population-genetics considerations:
  - Drift process (the coalescent)
  - Selection
  - Genome organization (linkage, gene order, gene families, etc.)
  - Population structure (isolation, inbreeding, migration, etc.)
- Both stochastic and deterministic forces are critical to understanding genes in populations
- Be wary of verbal explanations: the math has to work!