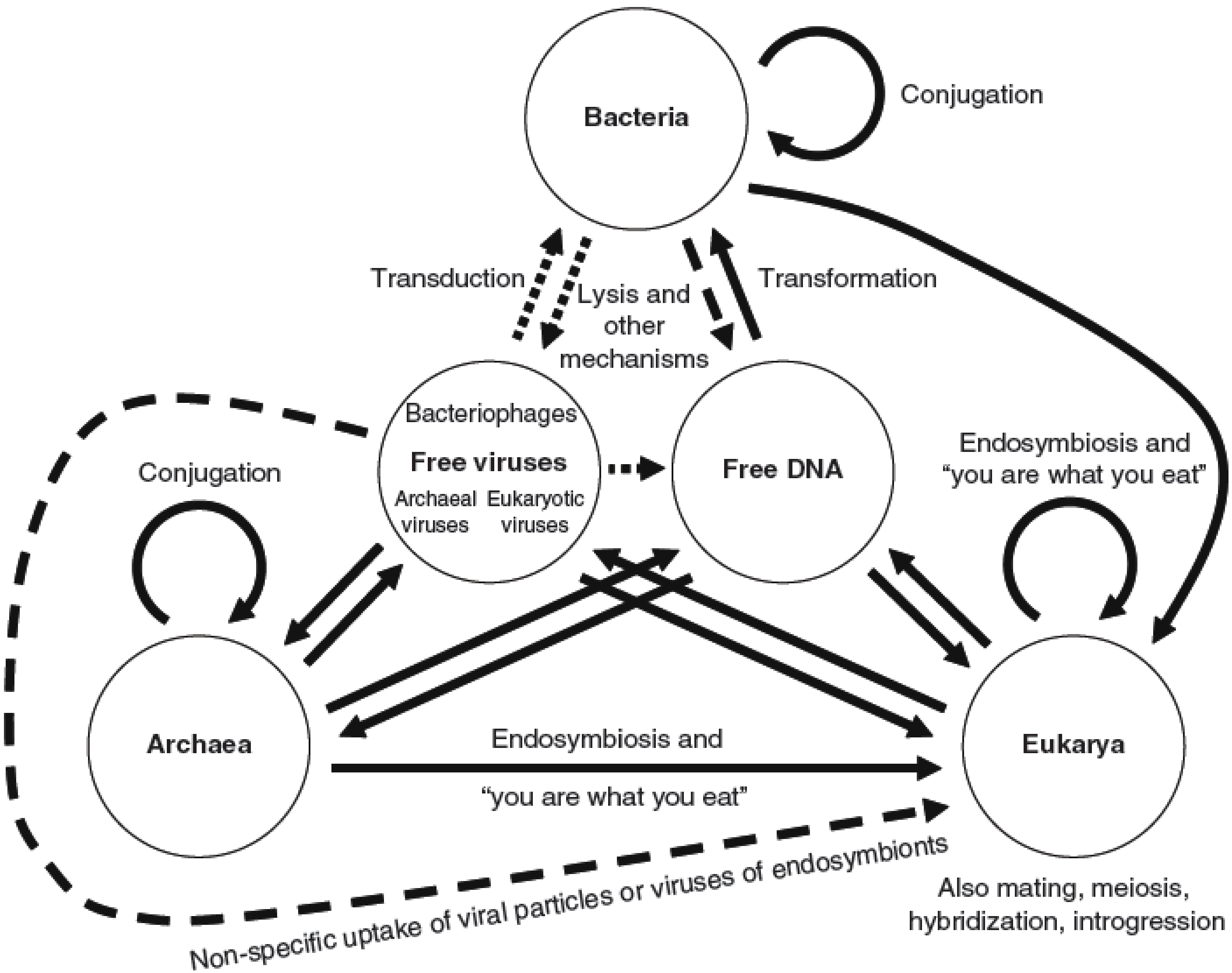
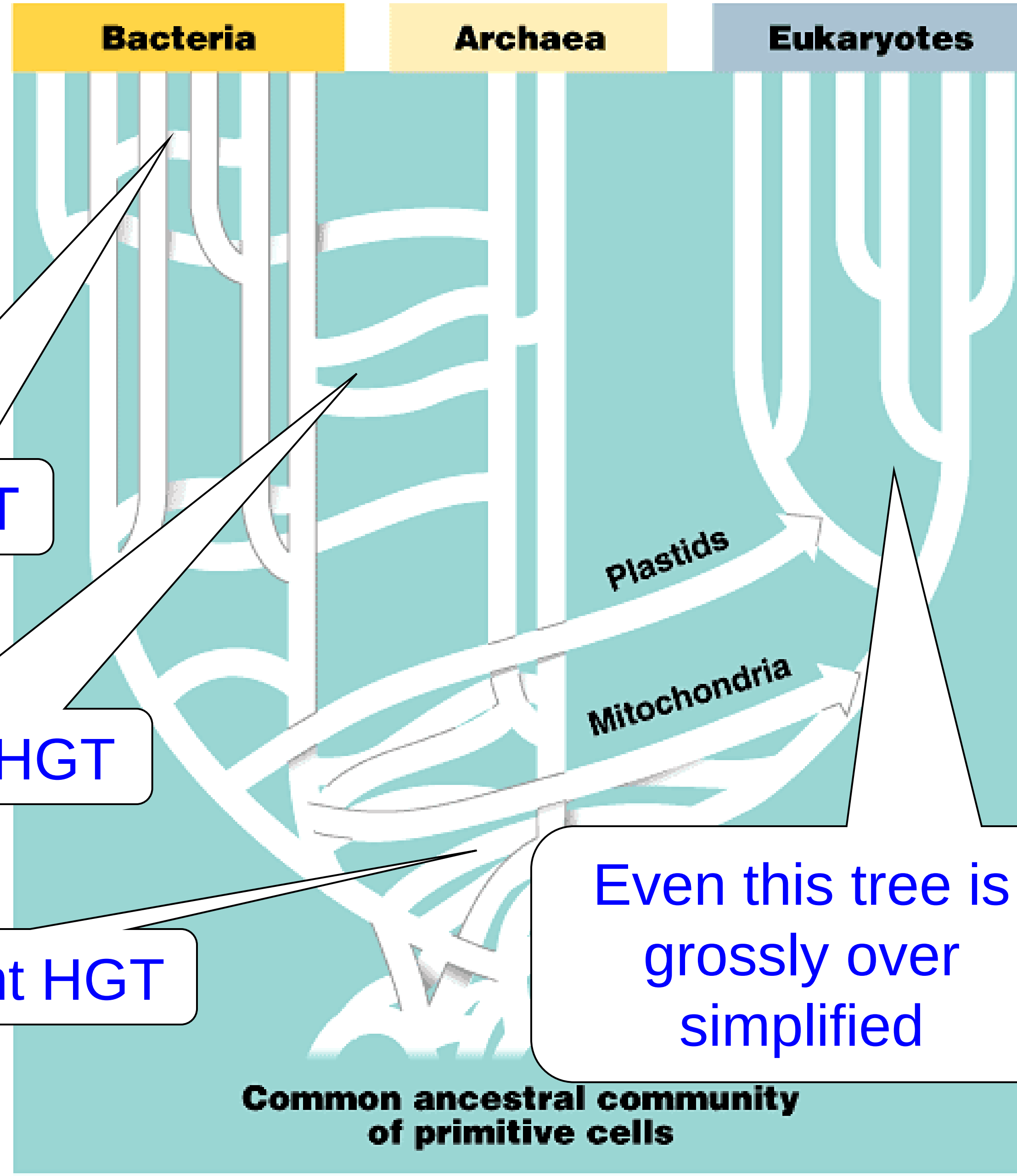
Gene Exchange

Pathways of Gene Exchange



Abedon, 2009

Universal Tree with HGT



"Modern" HGT

More recent HGT

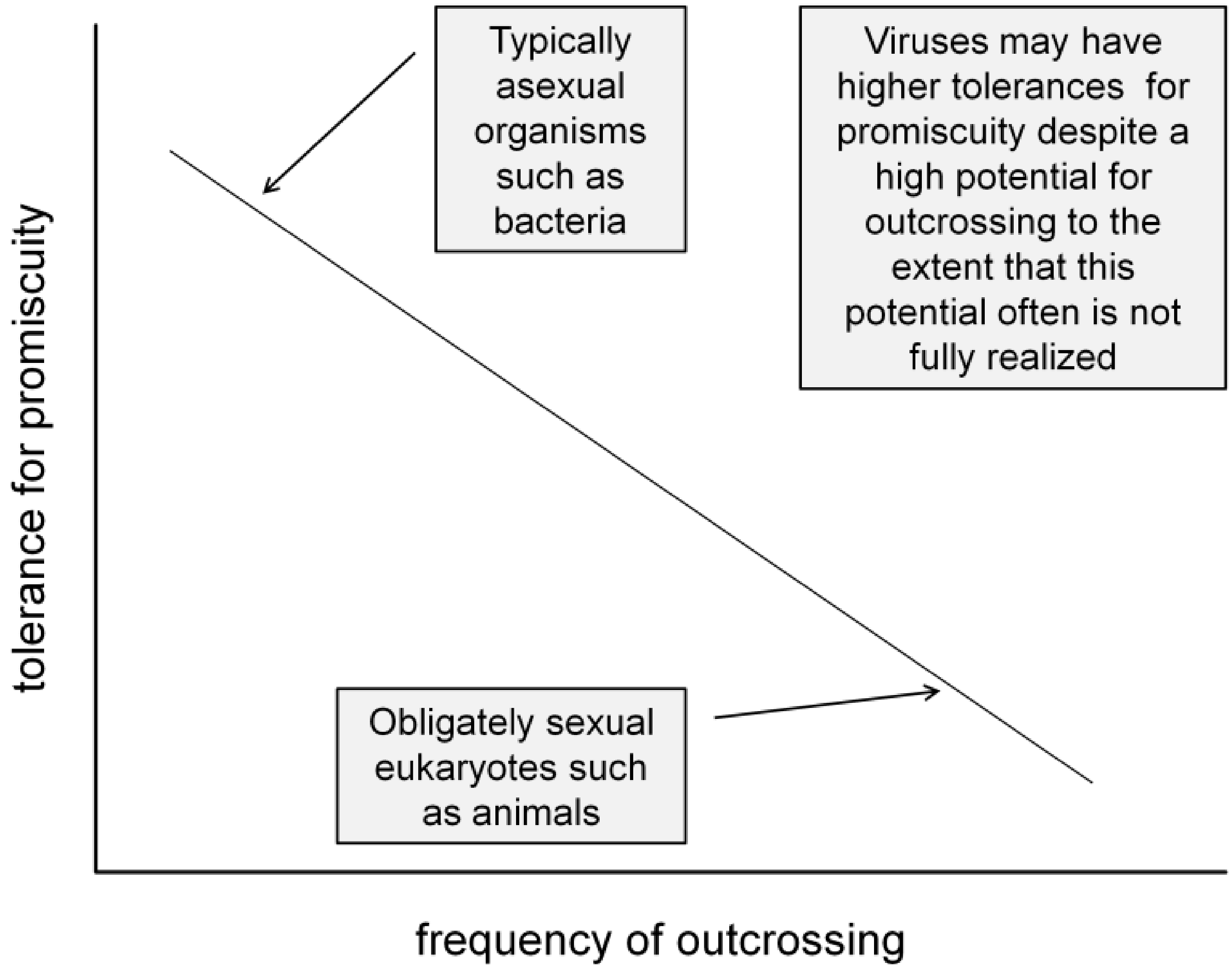
Ancient HGT

Even this tree is grossly over simplified

Variation in Sex/Gene Exchange

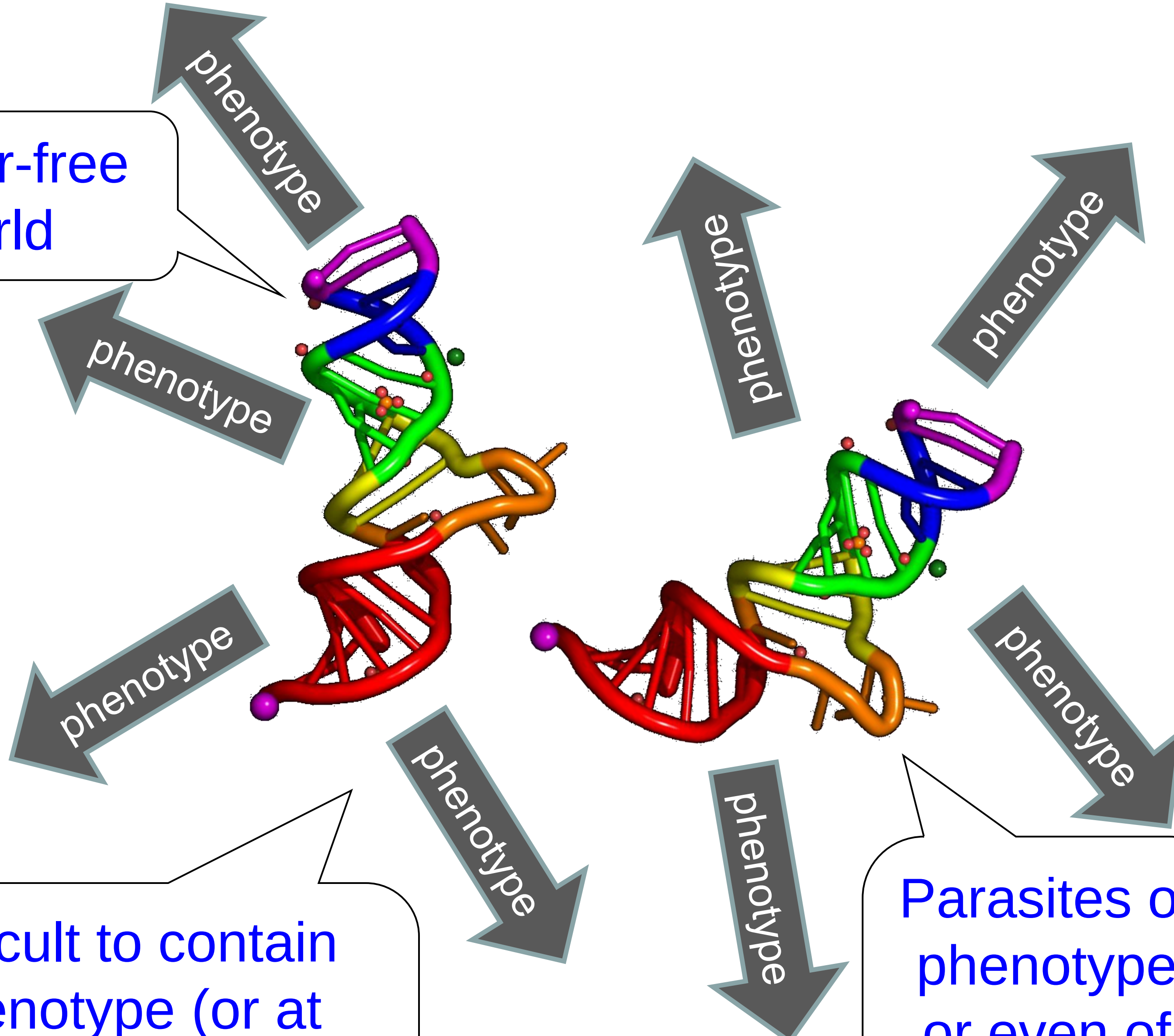
- Sex/gene exchange can occur by 2 distinct routes:
  - More or less equal contribution of genetic material, such as seen in many sexual cycles
  - Unequal contribution of relatively small amounts of genetic material to one individual (bacteria)
- Even in eukaryote sexual cycles, syngamy (fertilization) may or may not be followed by mitosis, i.e., may or may not be obligately reproductive
- Prokaryote sex always is not obligately reproductive
- Viral sex often accompanies viral reproduction, but viral reproduction usually is not obligately sexual
- Gene exchange via plasmids occurs without molecular recombination (but is still genetic recombination)
- In viruses, gene exchange can be via molecular recombination, reassortment, or by both mechanisms

Sex Both Limits and Promotes Diversity



Phenotype Sharing

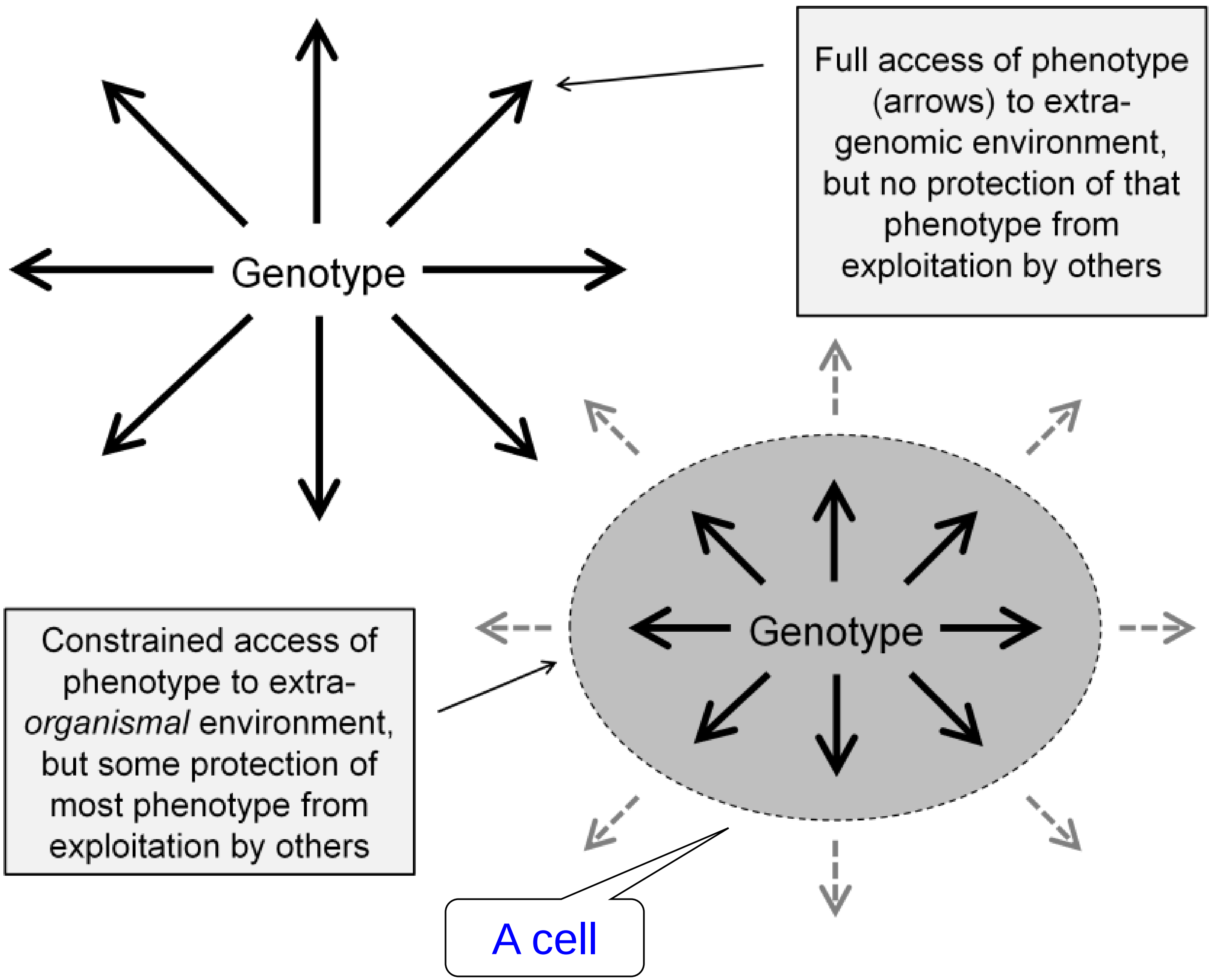
Barrier-free world



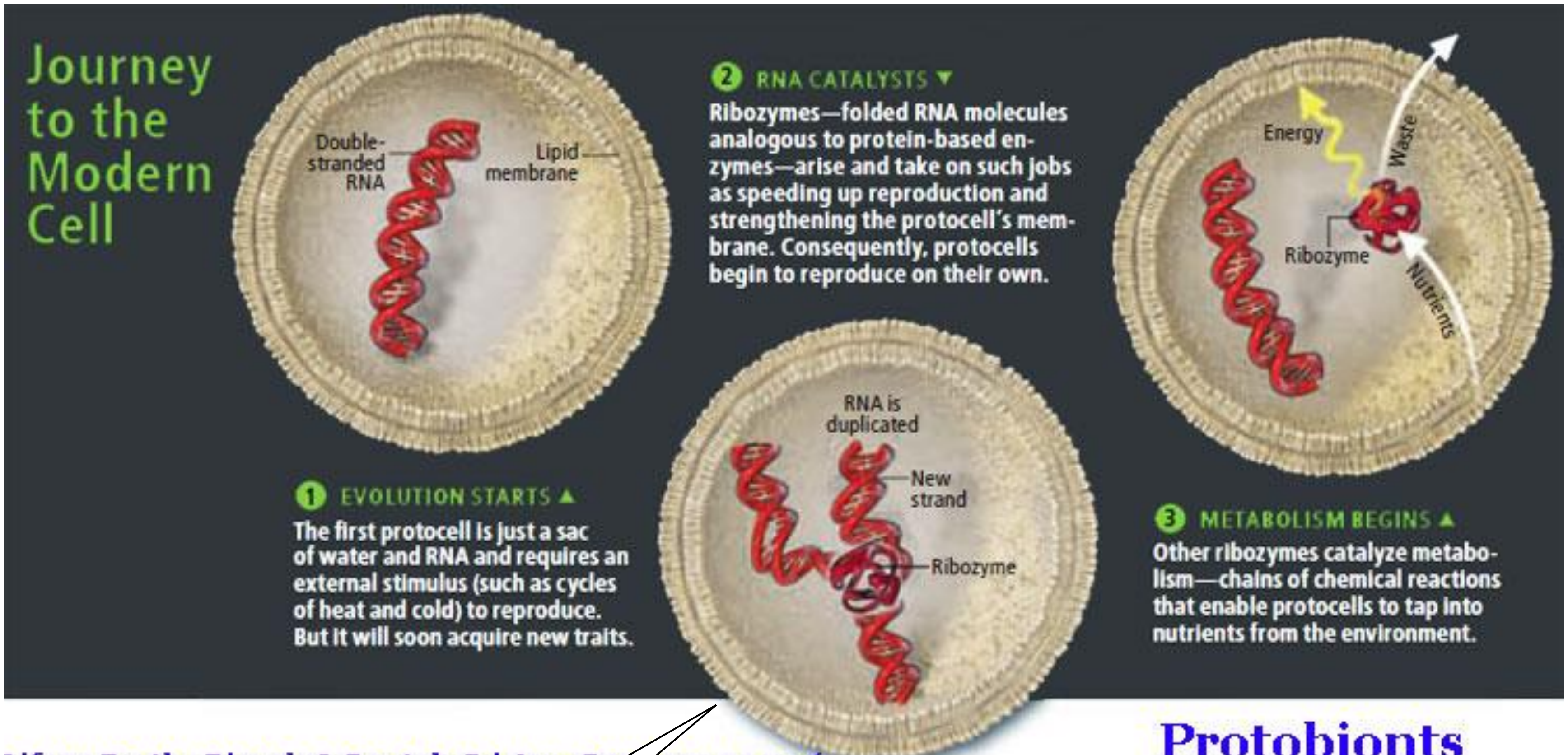
Difficult to contain phenotype (or at least products of phenotype)

Parasites of phenotype or even of genotype rampant?

Costs & Benefits of Barriers



Individuality: Barriers to Gene Transfer



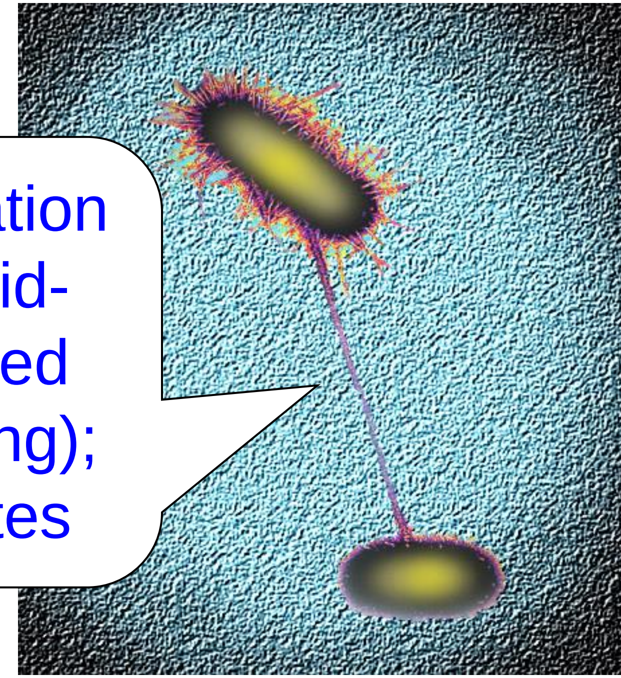
Life on Earth - Ricardo & Szostak, Sci.Am., Sep 2009, pg 54- 61.

Protobionts

Keeping one's phenotype to one's self

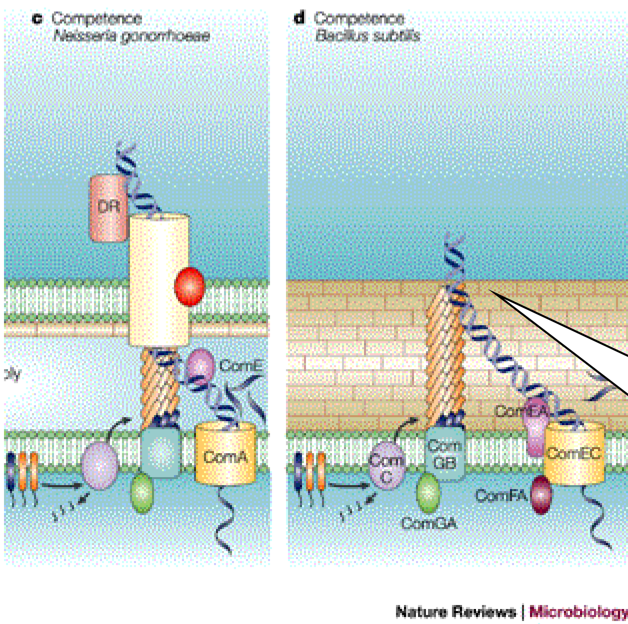
Protection against parasites, but also blocks genotype sharing, and limits nutrient acquisition?

Breeching of Barriers



Conjugation (plasmid-mediated breeching); Parasites

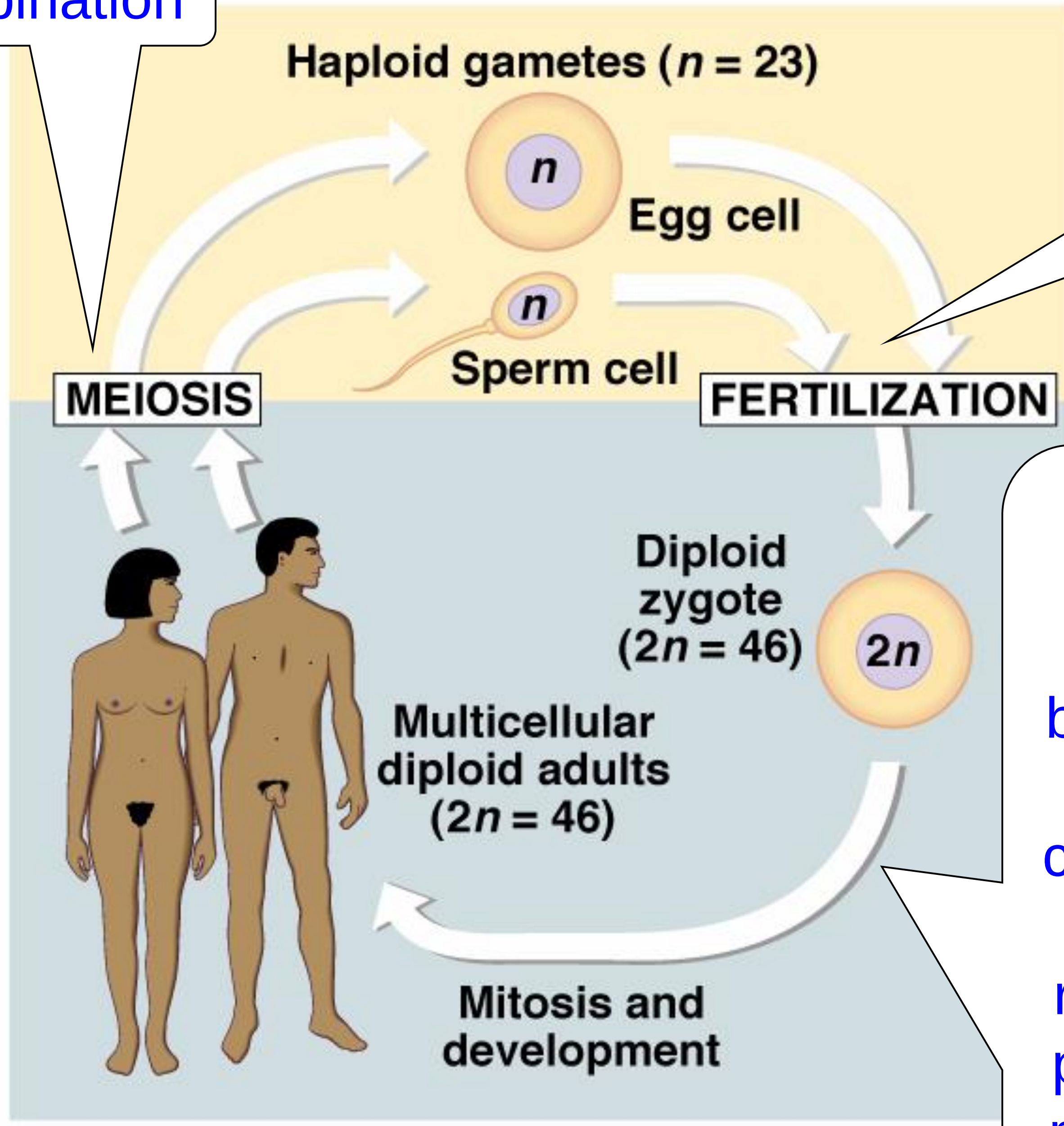
Transduction (virus-inflicted breeching); Consequence of parasitism



Transformation (self-inflicted breeching); Form of nutrient acquisition?

Really Big Breeching

Recombination



Really big breech

Big-time mixing of genotype, but demands genotype conservatism (else recombinant products are mostly toast)

Processes / Terms

- Molecular recombination is the breaking and joining of DNA (meiosis crossing over equivalent)
- Independent assortment or reassortment involves the mixing up of chromosomes or genomic segments originating from different parents (part of genetic recombination)
- Gene exchange and gene transfer refer to the movement of especially smaller pieces of DNA from one organism to another
- Horizontal or lateral gene transfer can have the same meaning as gene exchange or simply gene transfer
  - Often, though, they have more interspecific (rather than intraspecific) sharing connotations
- Gene exchange can occur w/o subsequent recombination or reassortment (e.g., plasmids)
  - “Genetic” recombination involves either molecular recombination (“crossing over”) or independent assortment/reassortment

Sex in Bacteria: Overview of Process

"Sex…can be defined as the inheritance of DNA from any source aside from the parental cell." Narra & Ochman (2006)

"Snippet"

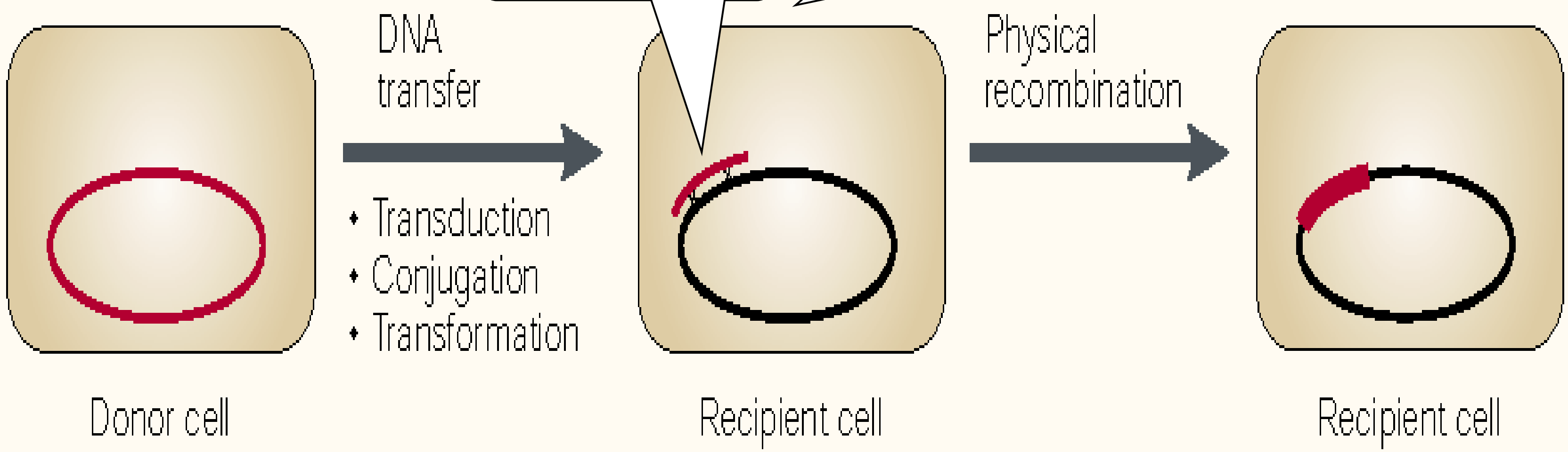
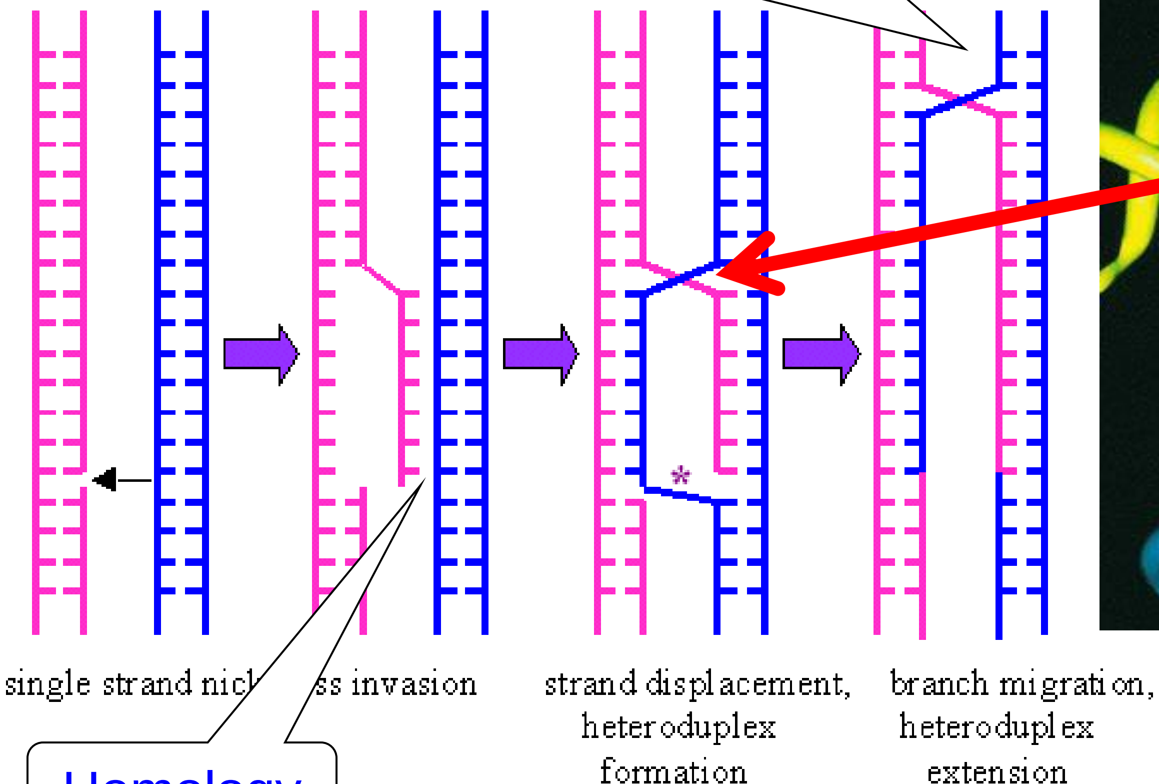


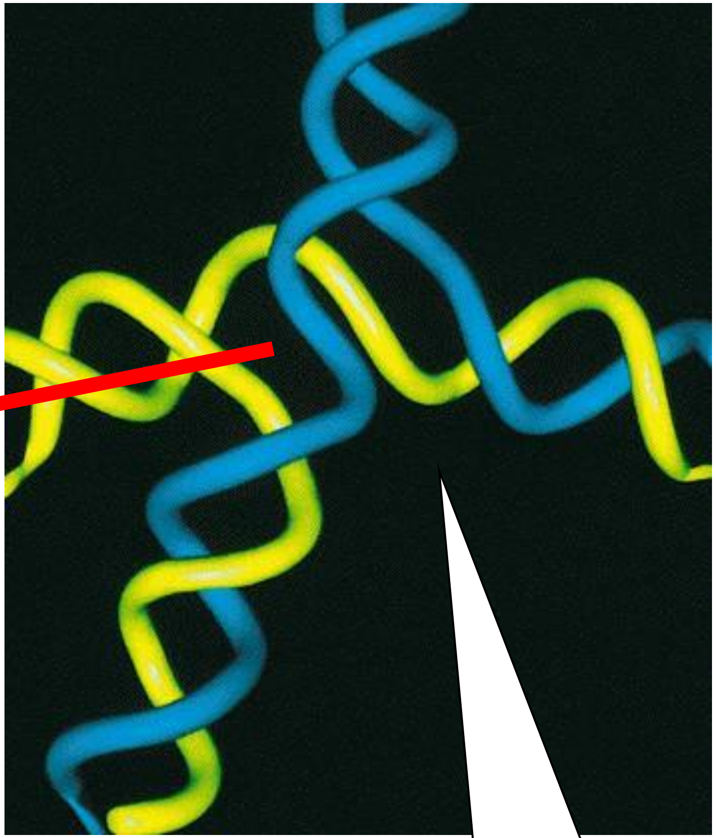
Figure 1 | **Genetic exchange in bacteria.** Transduction, conjugation and transformation can transfer a DNA fragment from a chromosome of a donor cell to a recipient cell. Physical recombination can then integrate this DNA into the recipient chromosome.

Molecular Recombination

Note creation of hybrid DNA, descending from two different parents



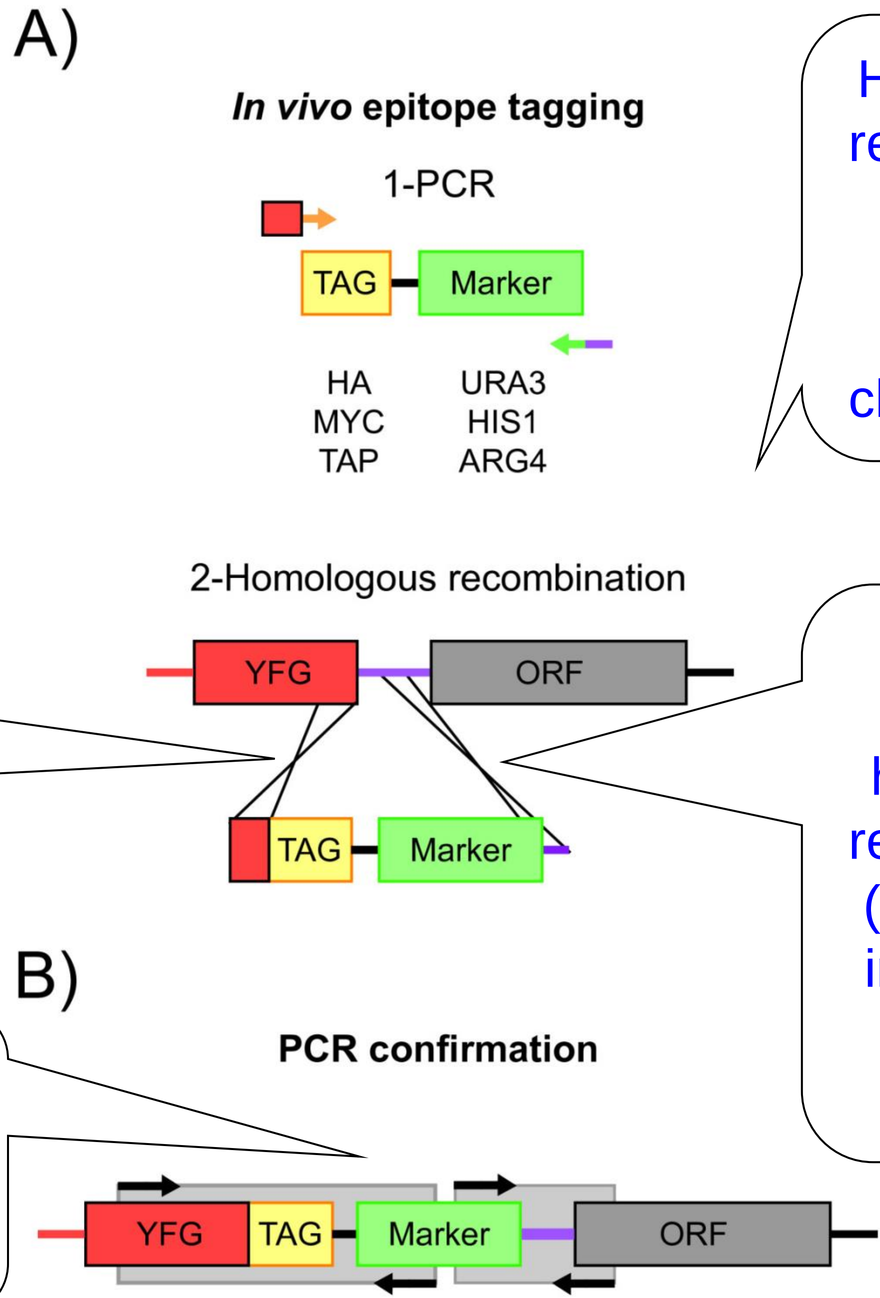
Homology



This is "close up" of a "Holliday" junction

http://www.clunet.edu/BioDev/omm/reca/frames/nick.htm
http://www.cbs.dtu.dk/staff/dave/roanoke/genetics980415f.htm

Insertions via Recombination



Heterologous recombination results in changes in sizes of chromosomes

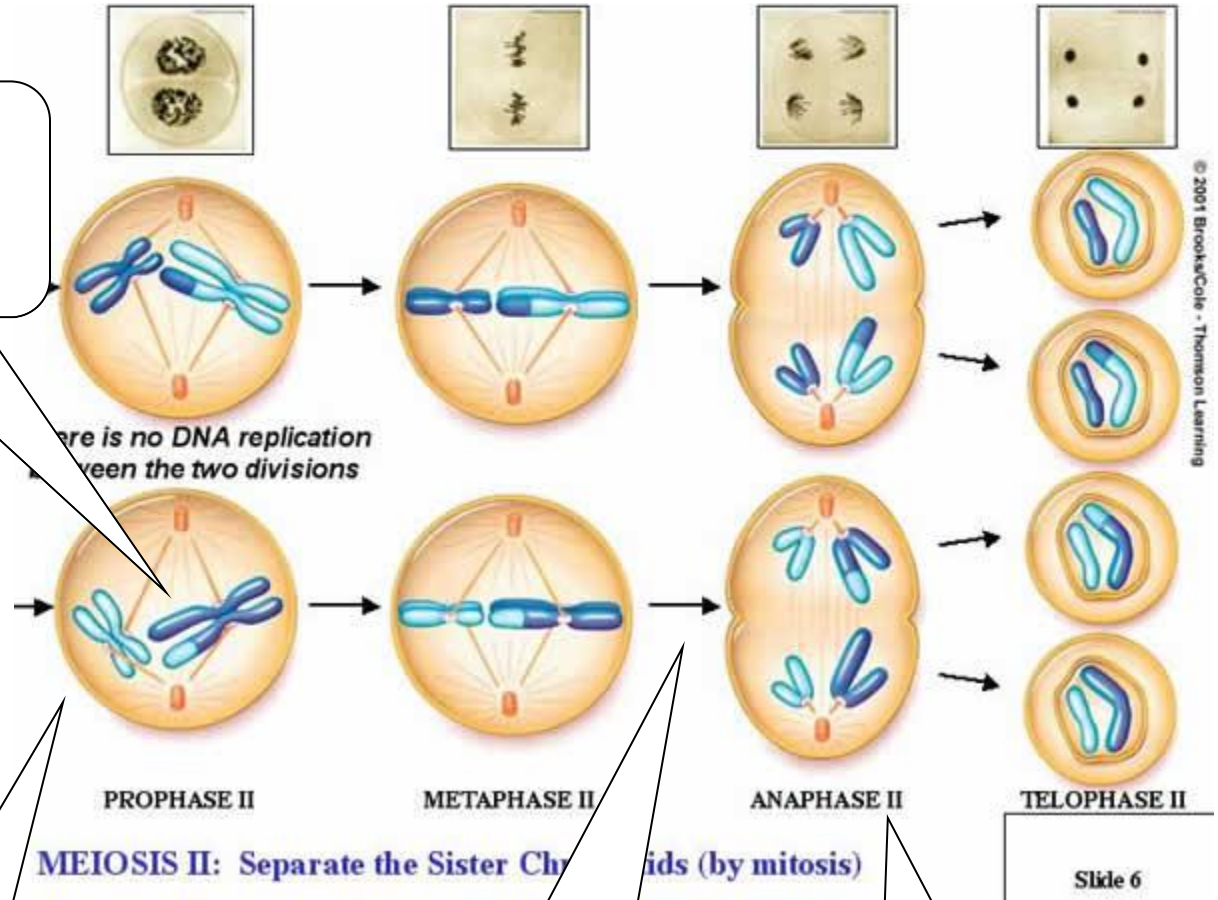
Full, partial, or micro homology

Illegitimate, a.k.a., non-homologous recombination (supposedly) involves little or no homology

Increase in amount of DNA/number of genes

Independent Assortment

Product of <u>homologous</u> recombination



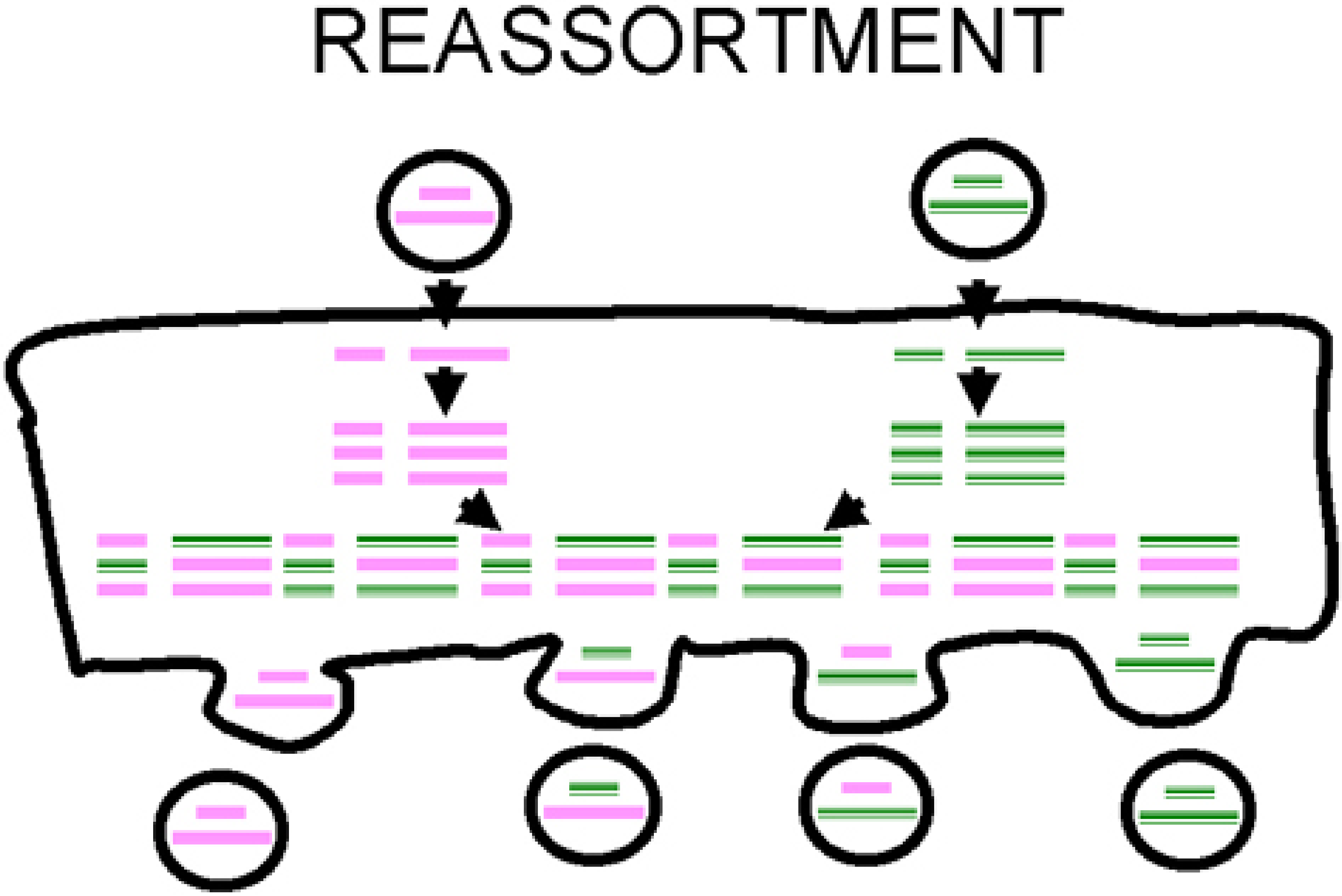
Products of recombination

Diploid to haploid transition

Independent assortment

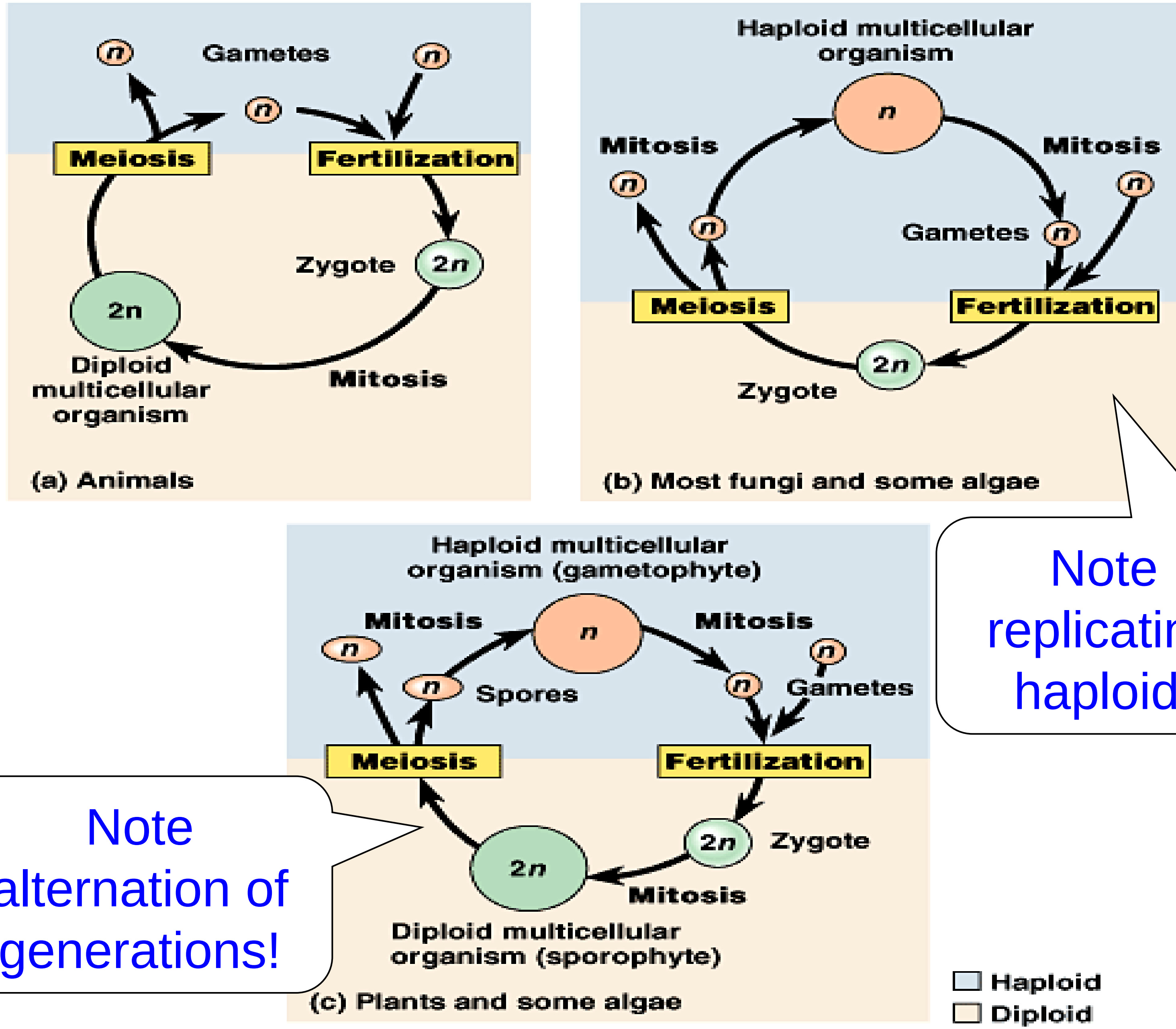
Genetic recombination does not necessarily involve molecular recombination

Viral Reassortment



http://pathmicro.med.sc.edu/mhunt/gen3.jpg

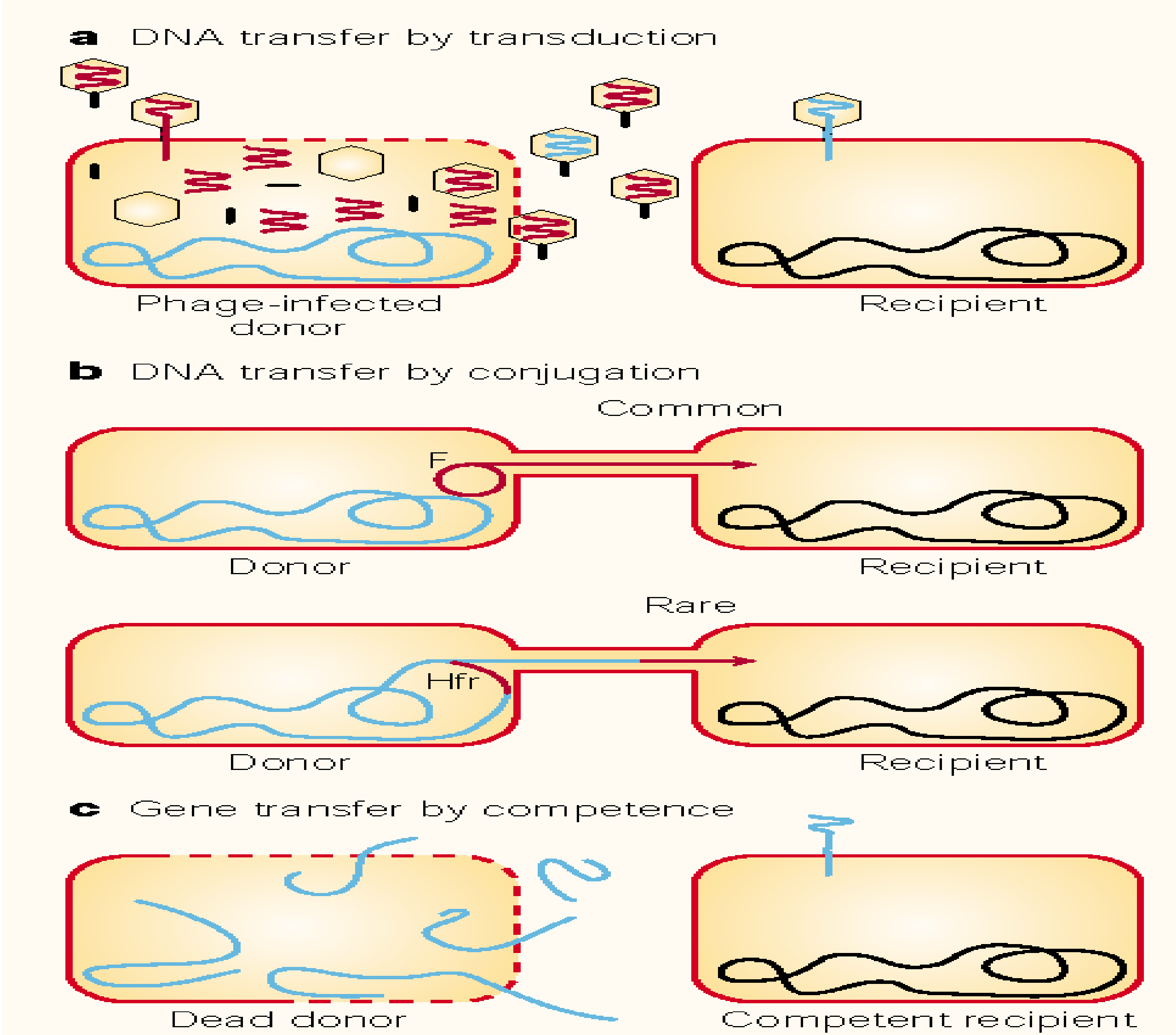
Variation in Sexual Cycles



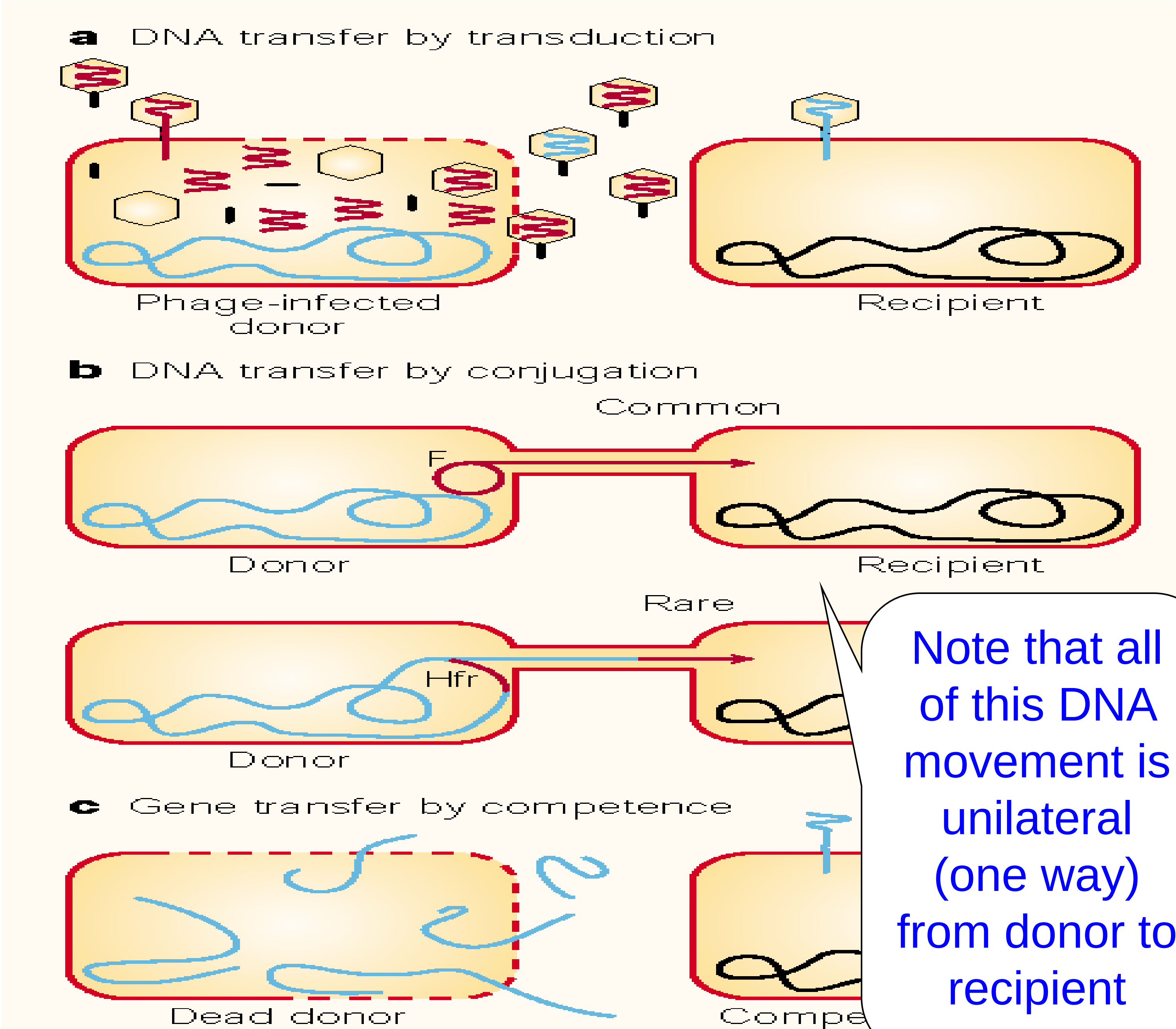
Note replicating haploid!

Note alternation of generations!

Bacteria Sexual Cycles

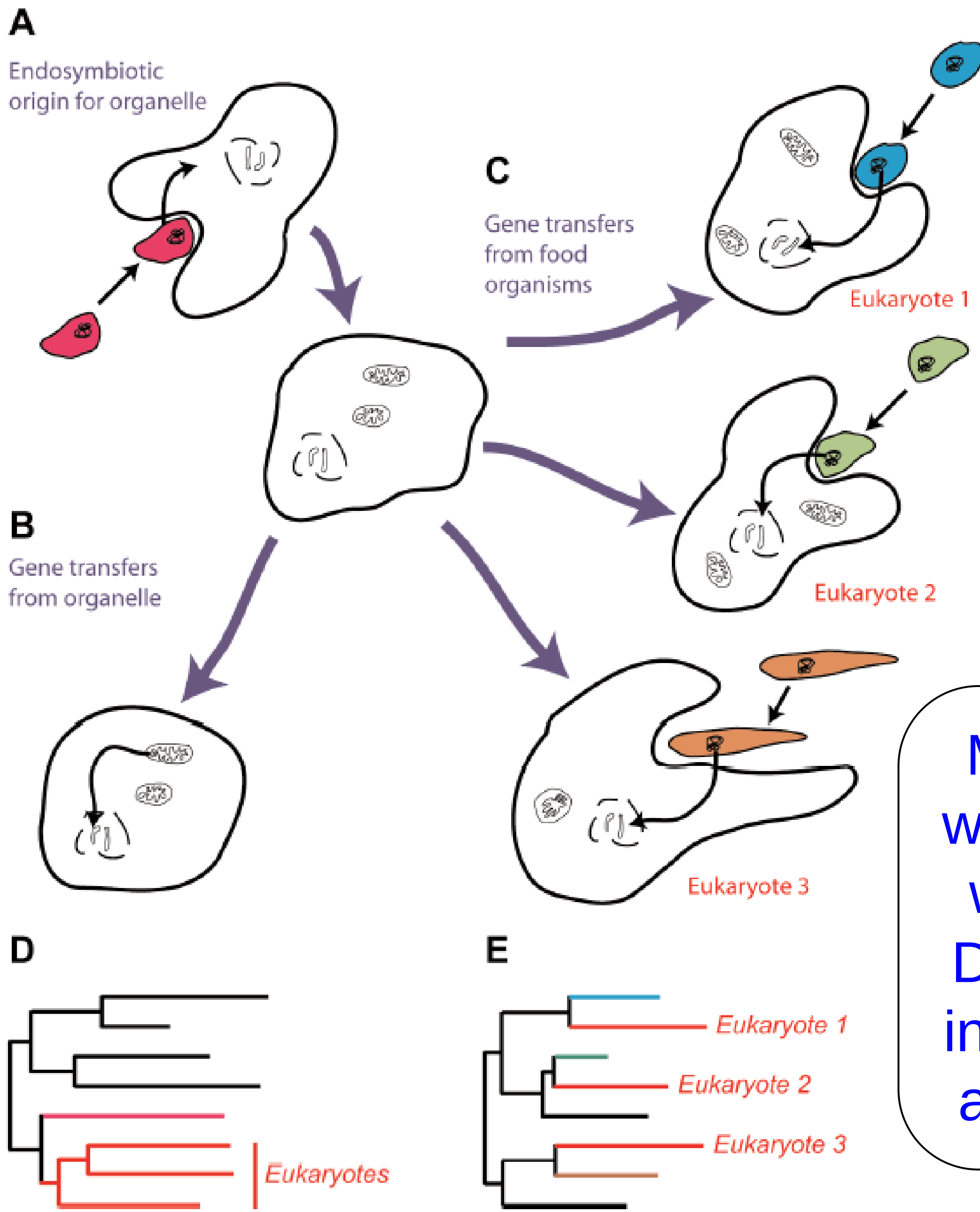


Bacteria Sexual Cycles



Note that all of this DNA movement is unilateral (one way) from donor to recipient

“You are what you eat”

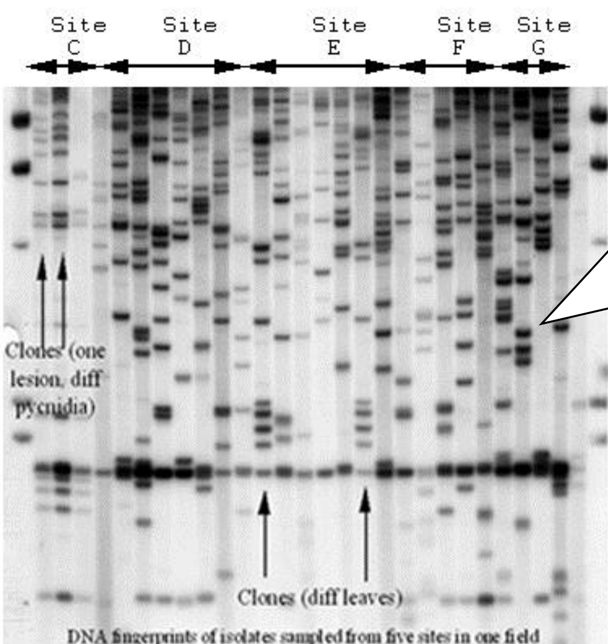


Andersson, 2005

Means, along with viruses, by which foreign DNA can enter into eukaryotes absent mating

Consideration of Clonality

- "All microbes can reproduce asexually and generate clones and clonal lineages.
- "Indeed, in natural populations of all microbial species examined (including viruses, bacteria, protozoa, algae, and fungi), evidence of clones and clonal lineages is abundant." Xu, 2004
- Establishing clonality can be important in determining the source/cause of epidemic disease

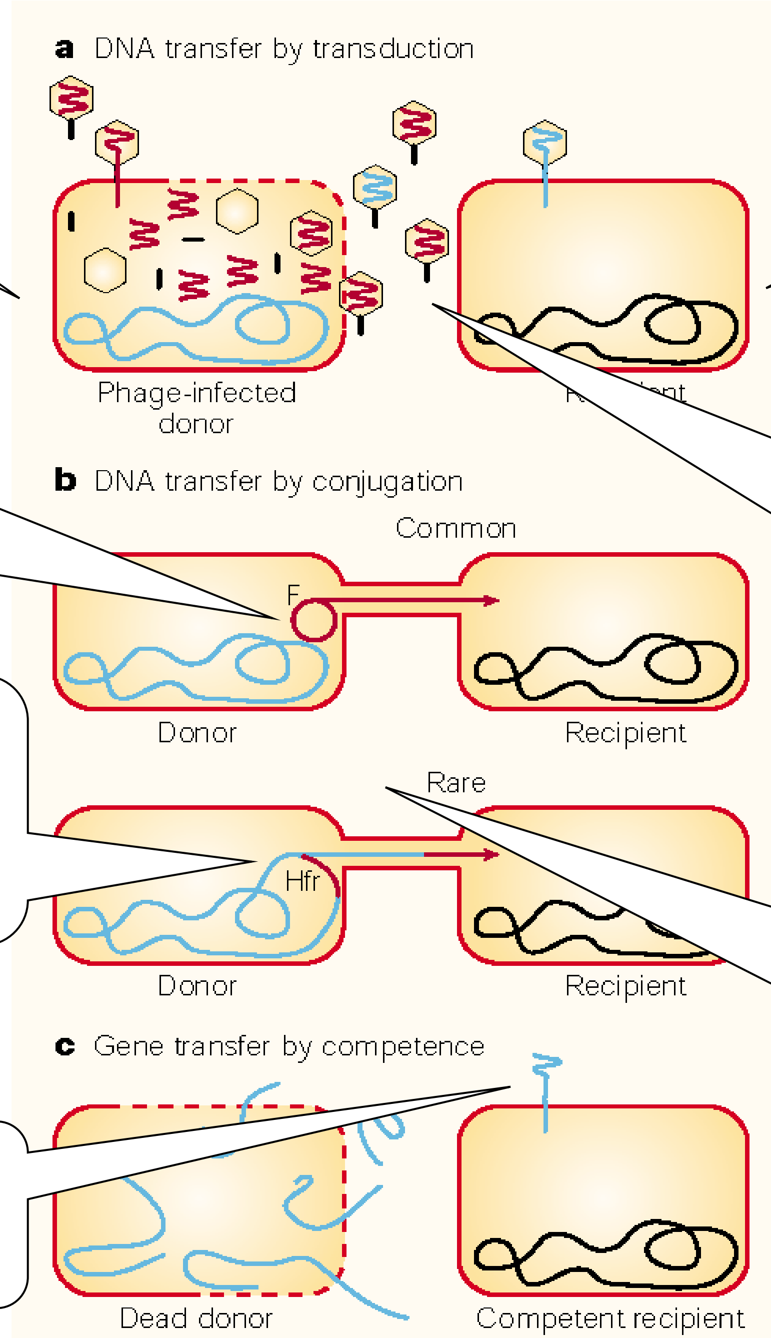


DNA fingerprints of *Mycosphaerella graminicola* isolates sampled from five sites separated by 10 m in one field. Clonality exists over spatial scales of a few meters within a field, but no clones are shared between fields

Focusing on Bacterial Sex

Donor cell

Recipient cell



Note no recombi-nation

Dependent on “infectious agents”

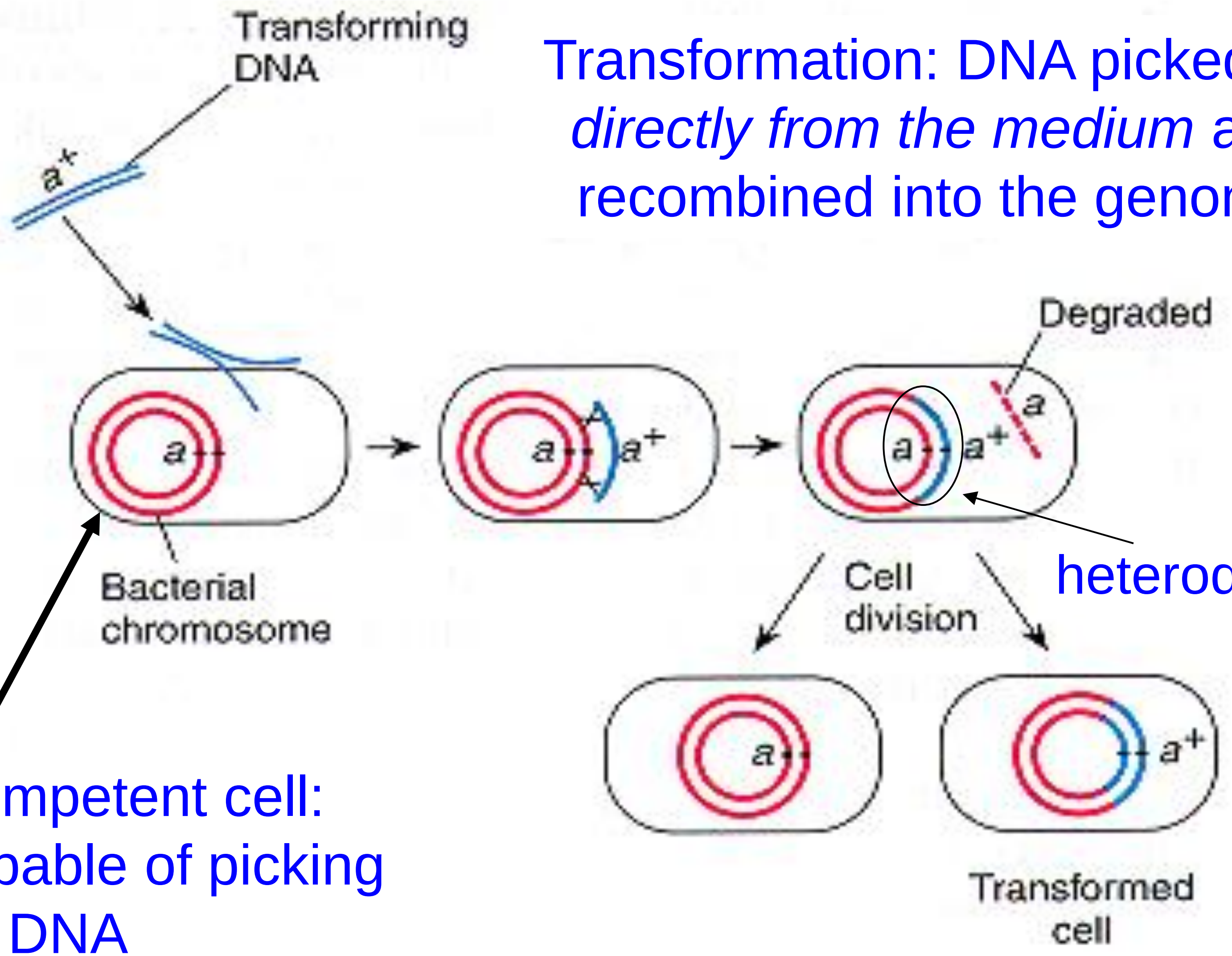
Recombi-nation, but Hfr is rare

Dependent on “infectious agents”

DNA as food?

Transformation

Transformation: DNA picked up *directly from the medium* and recombined into the genome



heteroduplex

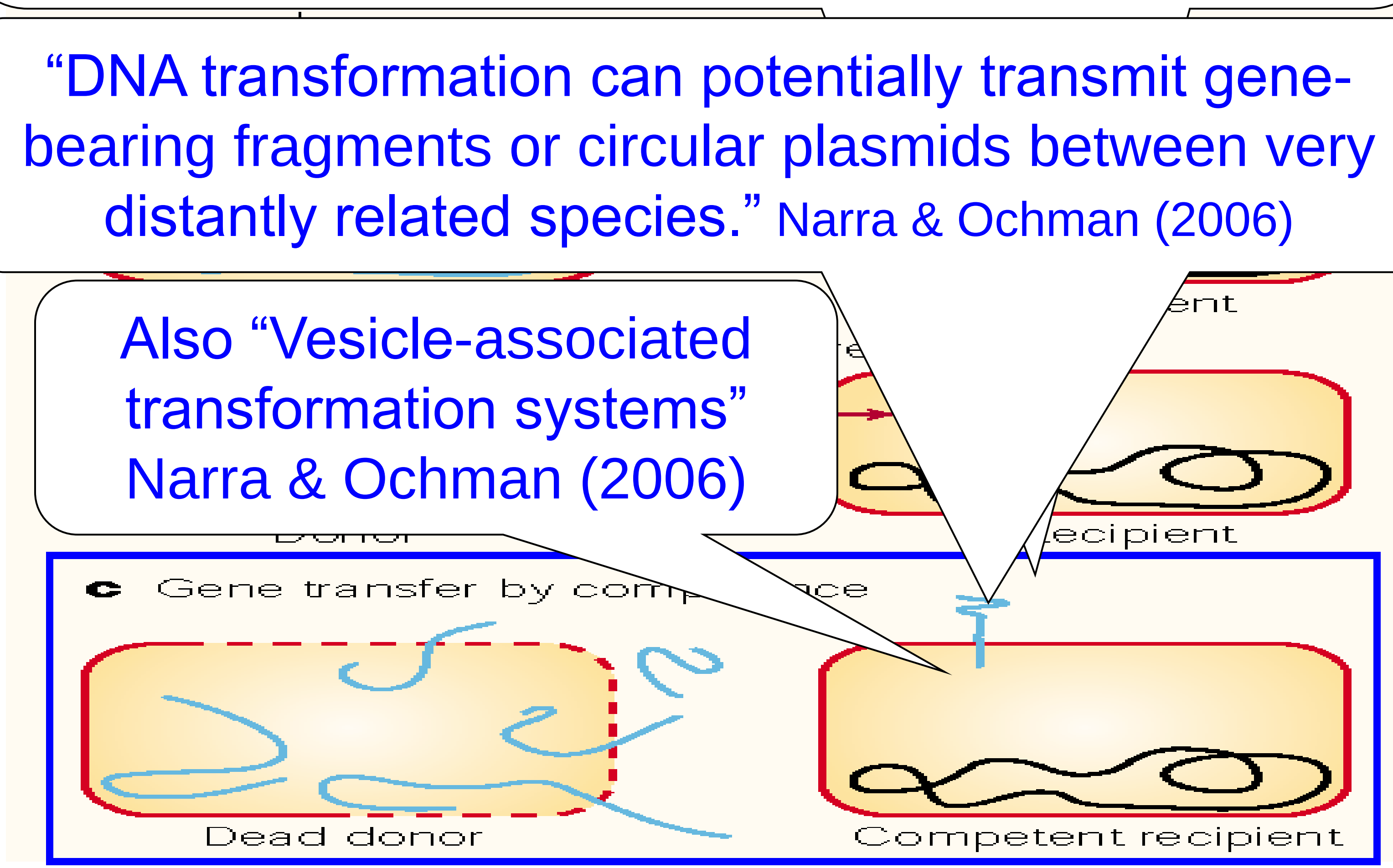
Competent cell: capable of picking up DNA

Transformation (competence)

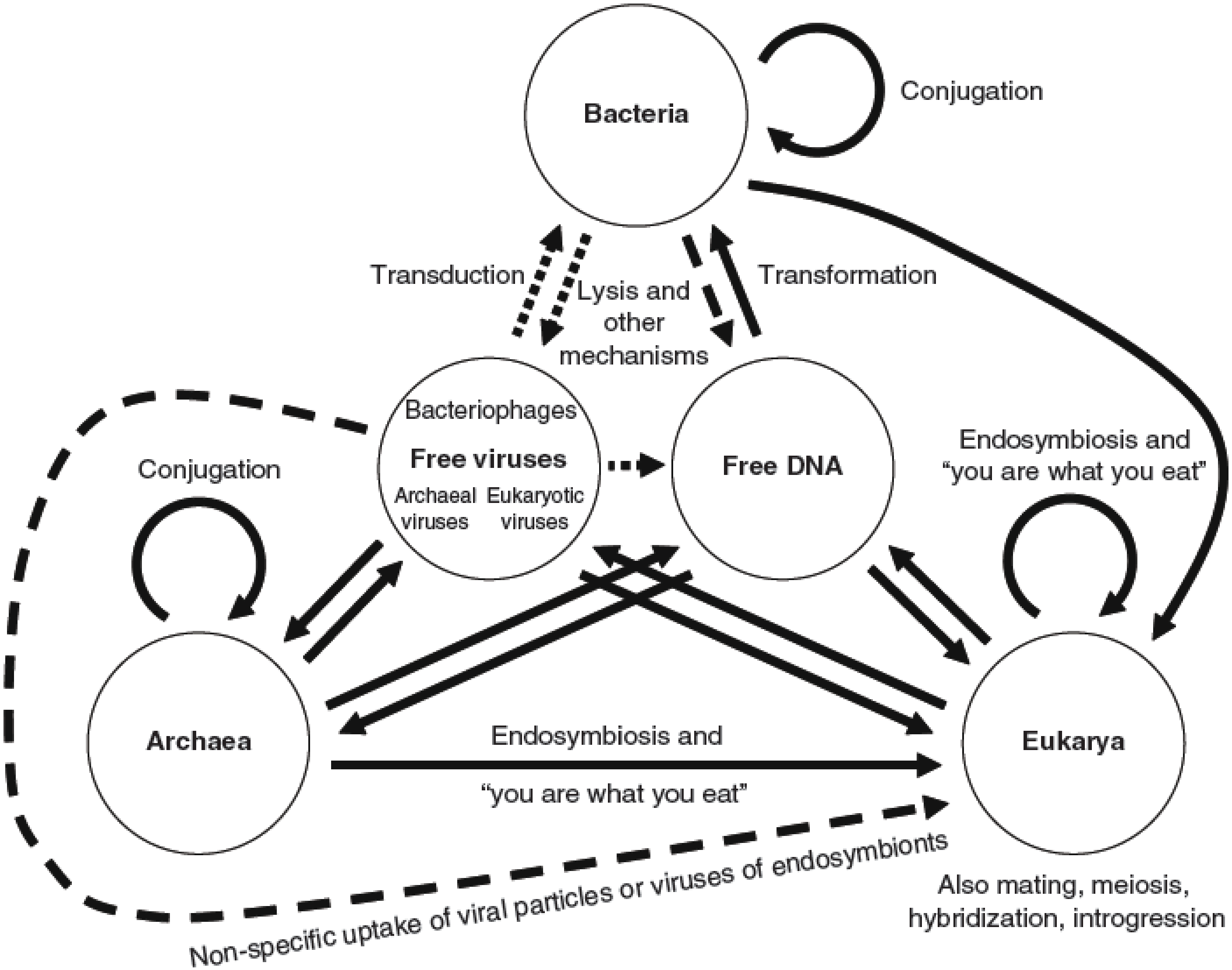
"Natural transformation… is the only mechanism that can potentially explain how bacteria acquire DNA from foreign species beyond the host range of mobile genetic elements or bacteriophages."
Thomas & Nielson (2006)

"DNA transformation can potentially transmit gene-bearing fragments or circular plasmids between very distantly related species." Narra & Ochman (2006)

Also "Vesicle-associated transformation systems"
Narra & Ochman (2006)



Pathways of Gene Exchange

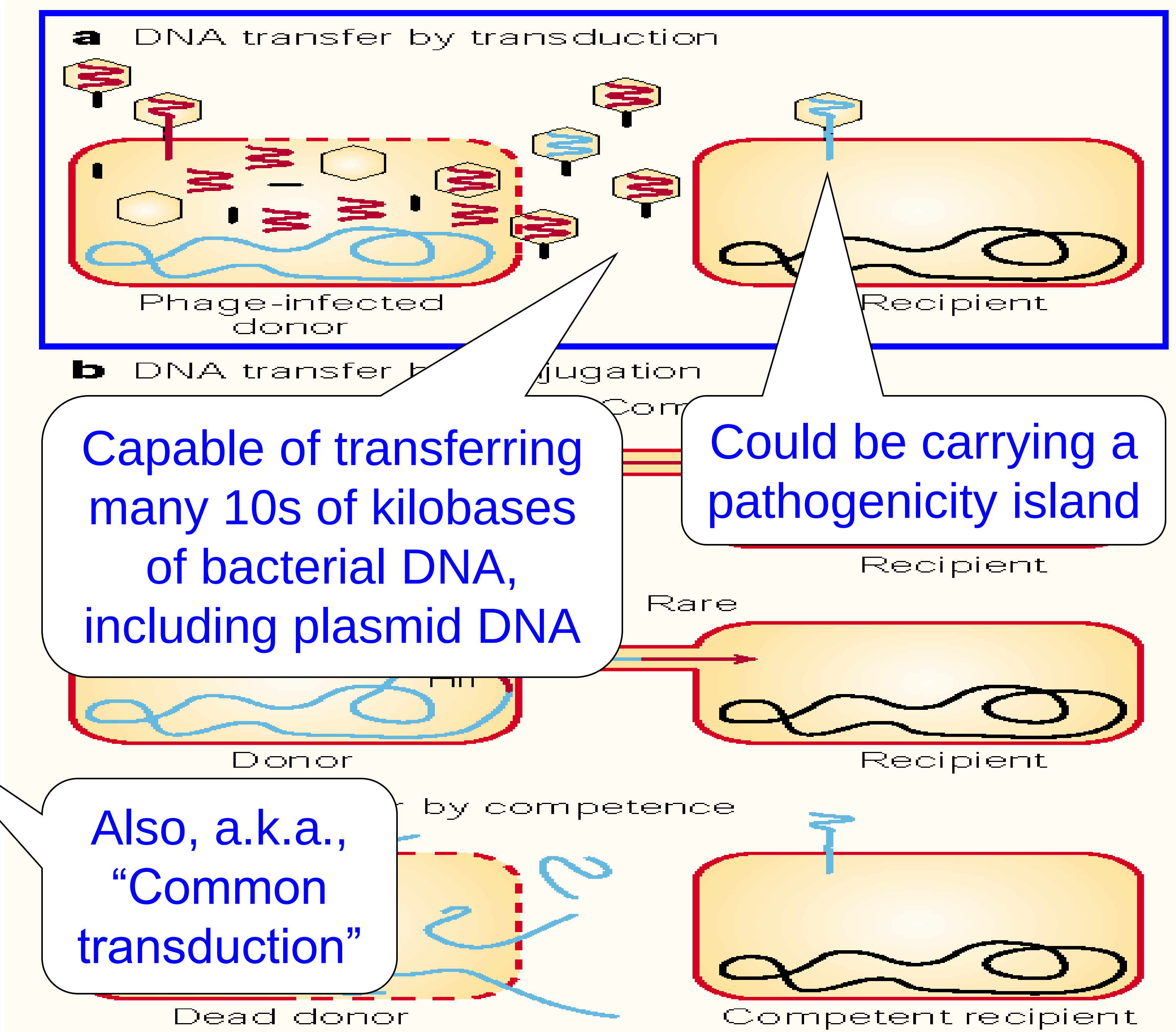


Abedon, 2009

3 Kinds of Transdcution

- Traditionally there are considered to be two kinds of transduction: generalized and specialized
  - Generalized transduction means that bacterial DNA but not phage DNA is transferred in a viral capsid (plasmid DNA also can be transferred)
  - Specialized transduction means that bacterial DNA is accidentally packaged along with phage DNA
- A sort of 3rd kind of “transduction” involves genes described as “Morons” (for “more” DNA) as phage parts
  - A moron is phage or bacterial DNA that is incorporated into a phage, presumably via illegitimate recombination
  - Can be virulence factors, such as exotoxin genes
- Moron acquisition is “specialized” in terms of carrying both viral and bacterial DNA
  - There is a fine line between moron and phage genes
  - Phages may have originated via “moron accretion”

Generalized Transduction

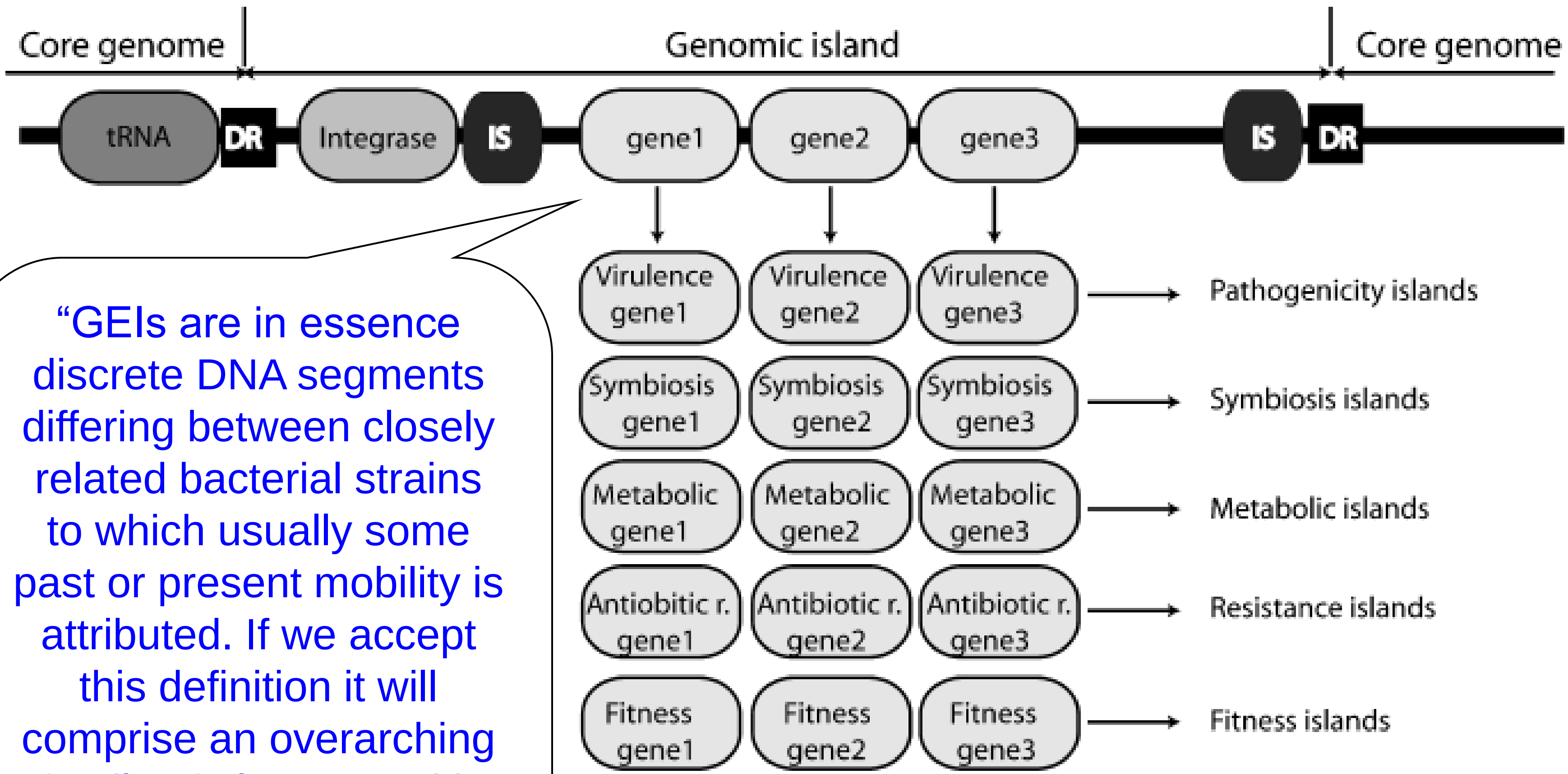


Capable of transferring many 10s of kilobases of bacterial DNA, including plasmid DNA

Could be carrying a pathogenicity island

Also, a.k.a., “Common transduction”

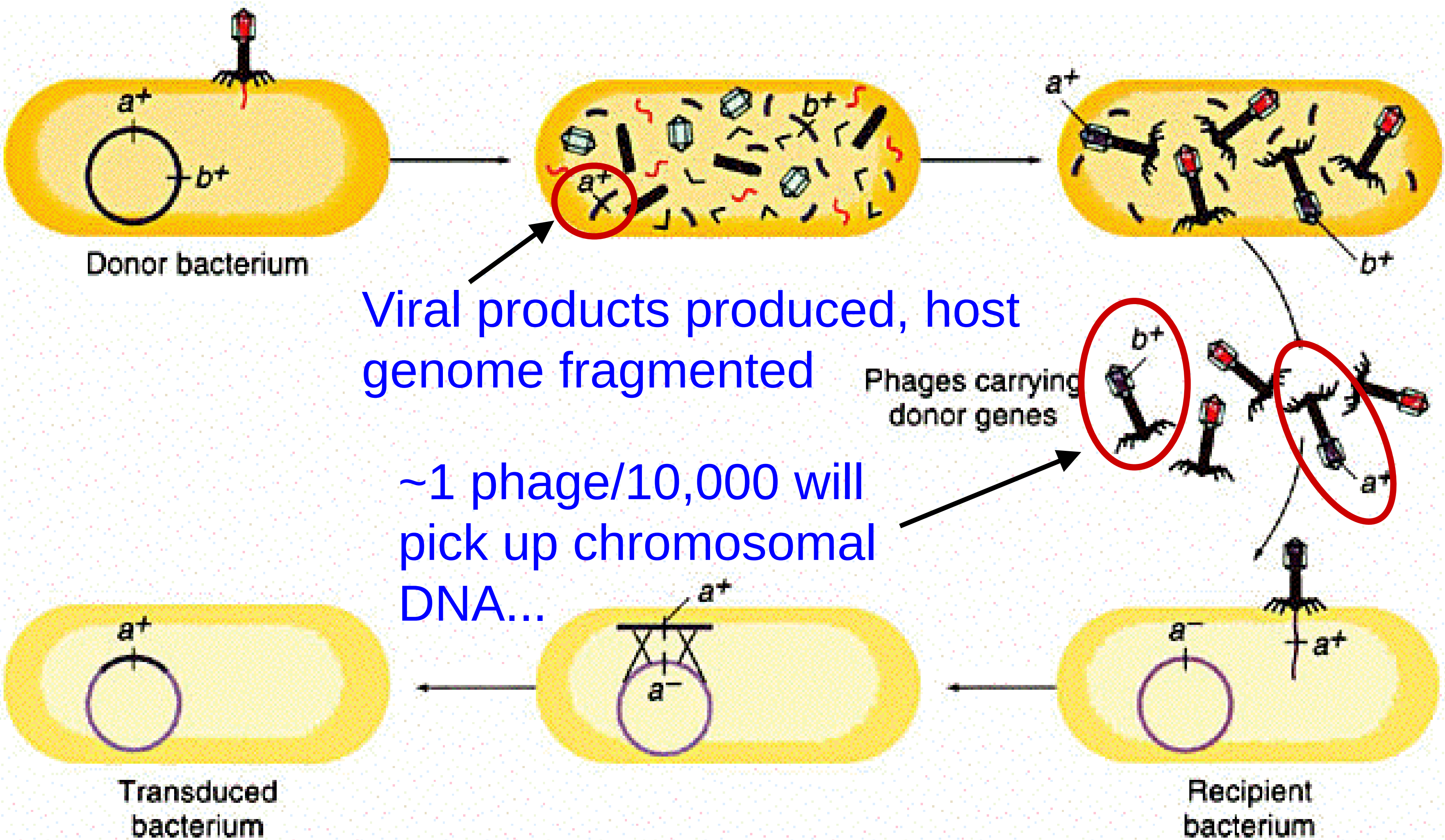
Variety of Genomic Islands (GEIs)



"GEIs are in essence discrete DNA segments differing between closely related bacterial strains to which usually some past or present mobility is attributed. If we accept this definition it will comprise an overarching family of elements with different functional life-styles."

Juhas *et al*. (2009)

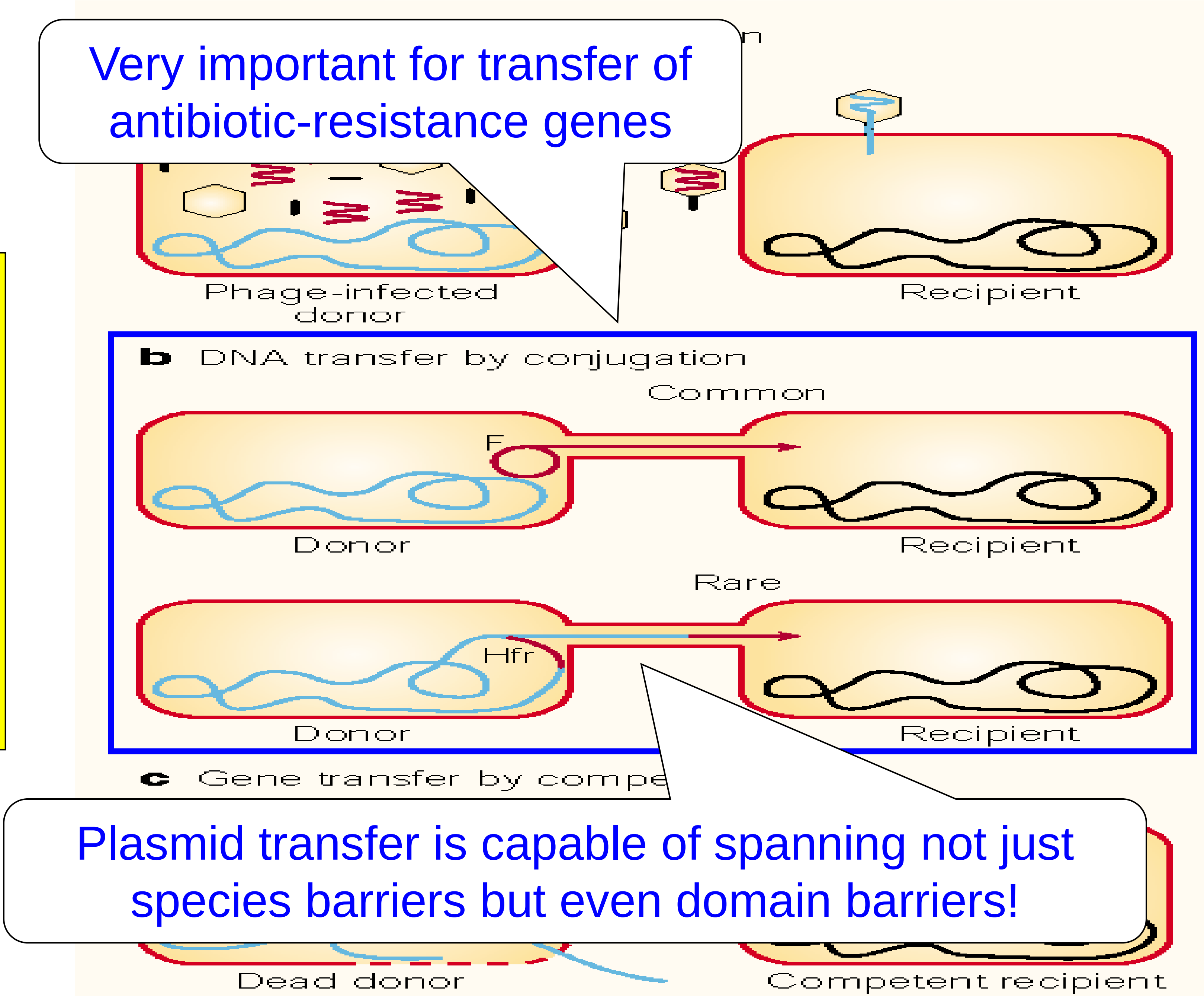
Generalized Transduction



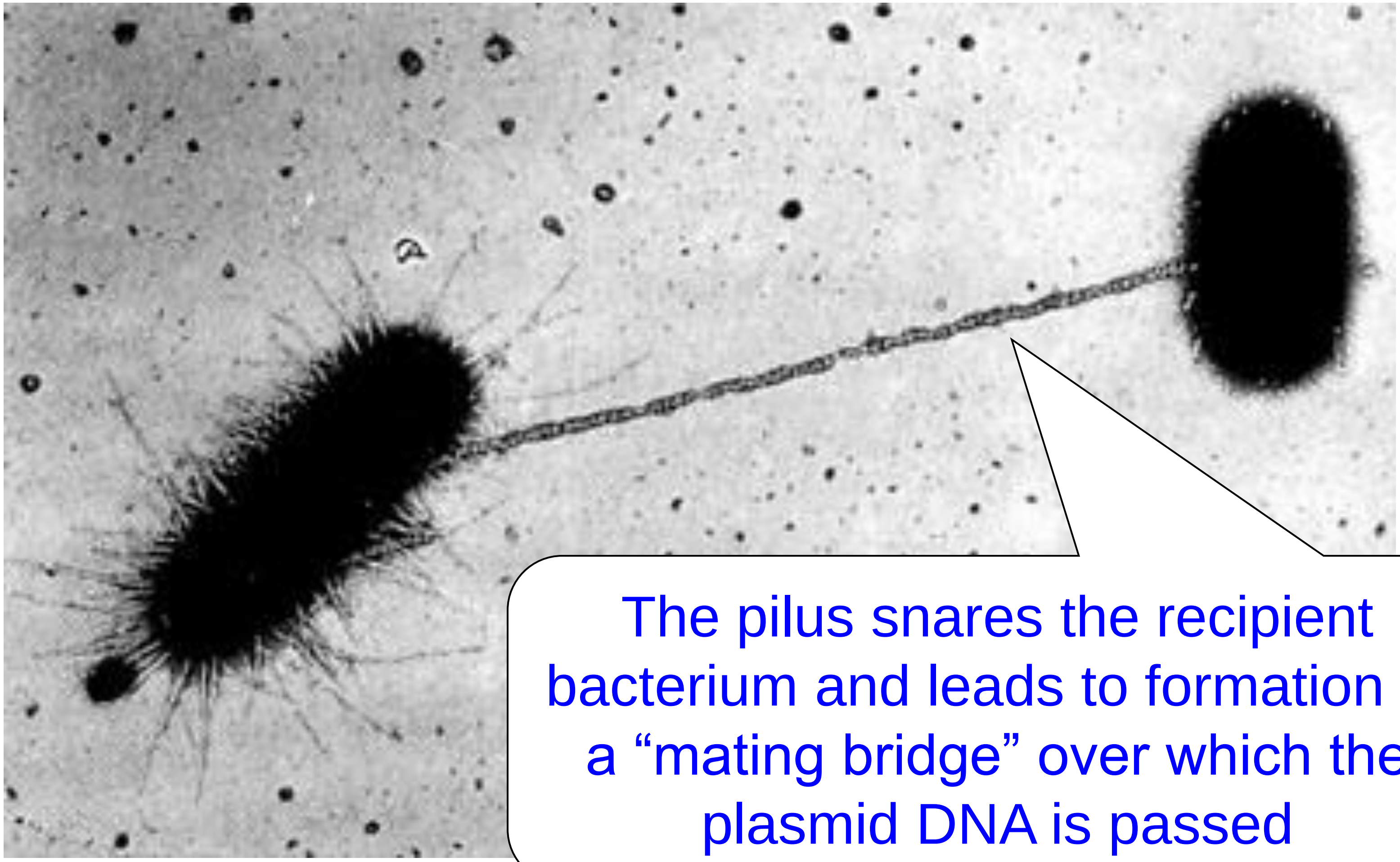
Viral products produced, host genome fragmented

~1 phage/10,000 will pick up chromosomal DNA...

Conjugation

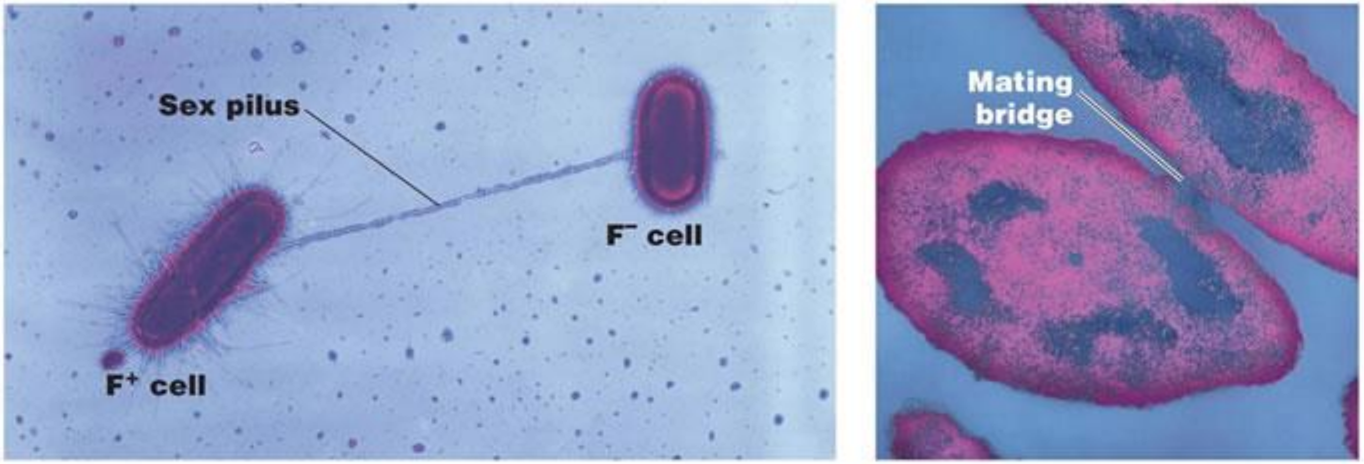


Conjugation: Sex Pilus

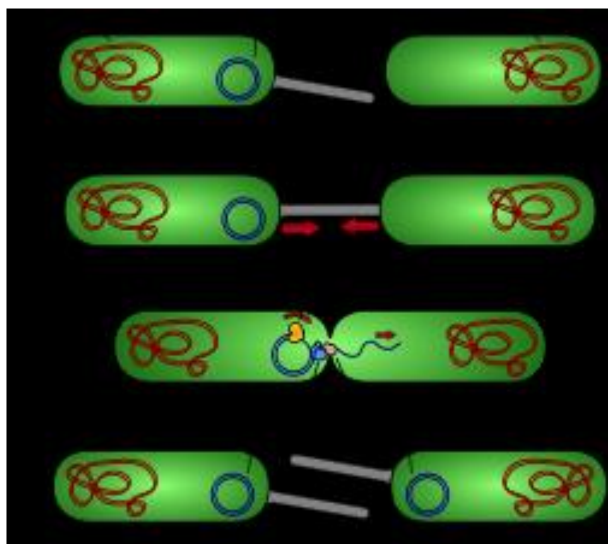


The pilus snares the recipient bacterium and leads to formation of a “mating bridge” over which the plasmid DNA is passed

Mating Bridge



(a) Sex pilus TEM 1 μm **(b)** Mating bridge TEM 0.3 μm

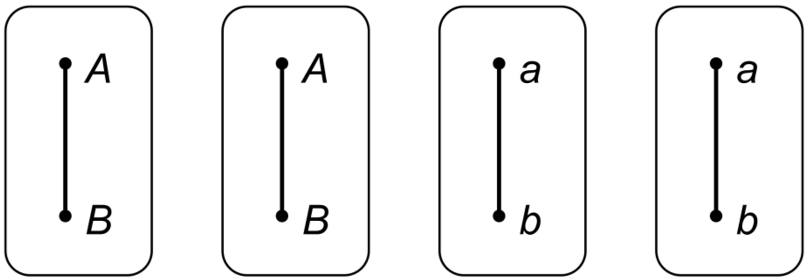


Linkage (between genes, and a whole lot more)

- Linkage is the physical binding together of two or more genetic loci
- This can include:
  - Close-together loci on the same chromosome
  - Loci found on the same chromosome: if no molecular recombination
  - Loci found on different chromosomes: if no assortment/reassortment and/or no sex
  - Loci found in separate organisms: if their reproduction is "linked"
- Linkage is actually an even more broadly applicable concept, e.g.,
  - The fact that your car and your car keys are not linked can be an ongoing problem!
  - Linkage, at some level, can be important for the evolution of cooperation
  - Multicellularity both represents a form of linkage and is dependent on this linkage being evolutionarily stable

Linkage Disequilibrium

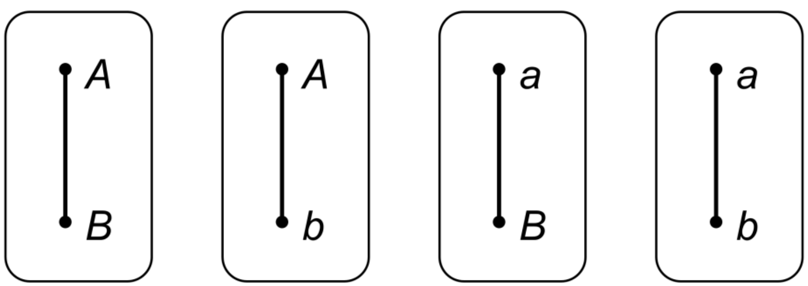
Linkage Disequilibrium



Results from:

- Non-random mating
- Rare sex
- Spatial structure
- Well-isolated sub-populations

Linkage Equilibrium



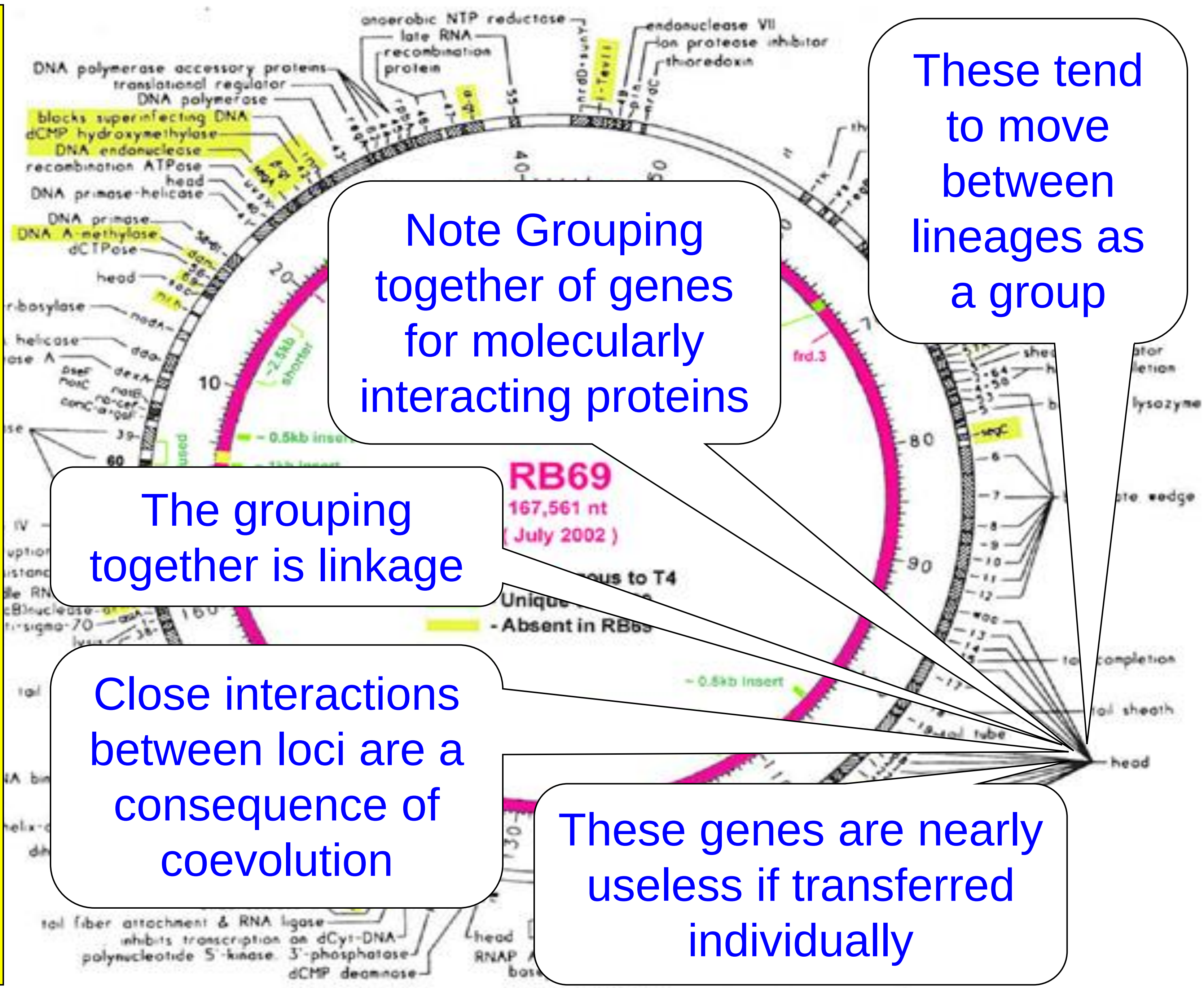
Results from:

- Random mating
- Frequent sex
- Well-mixed environments
- Sub-populations in frequent communication

Linkage Disequilibrium

- Linkage disequilibrium refers to an absence of separation of linked alleles and implies an absence of sex (i.e., the presence of asexual/clonal reproduction)
- An absence of linkage disequilibrium, in turn, suggests an occurrence of sexual reproduction:
  - "…in purely asexual populations, alleles from genes in different parts of the genome should give identical evolutionary patterns among individuals in the population and should be in significant linkage disequilibria.
  - "In contrast, sex and sexual reproduction would break up these associations and generate linkage equilibrium. Therefore, linkage equilibrium and (or) genealogy incongruence among genes in natural microbial populations are consistent with genetic recombination and sexual reproduction in these populations." — Xu (2004)

Linkage and Coevolution of Alleles



Note Grouping together of genes for molecularly interacting proteins

These tend to move between lineages as a group

The grouping together is linkage

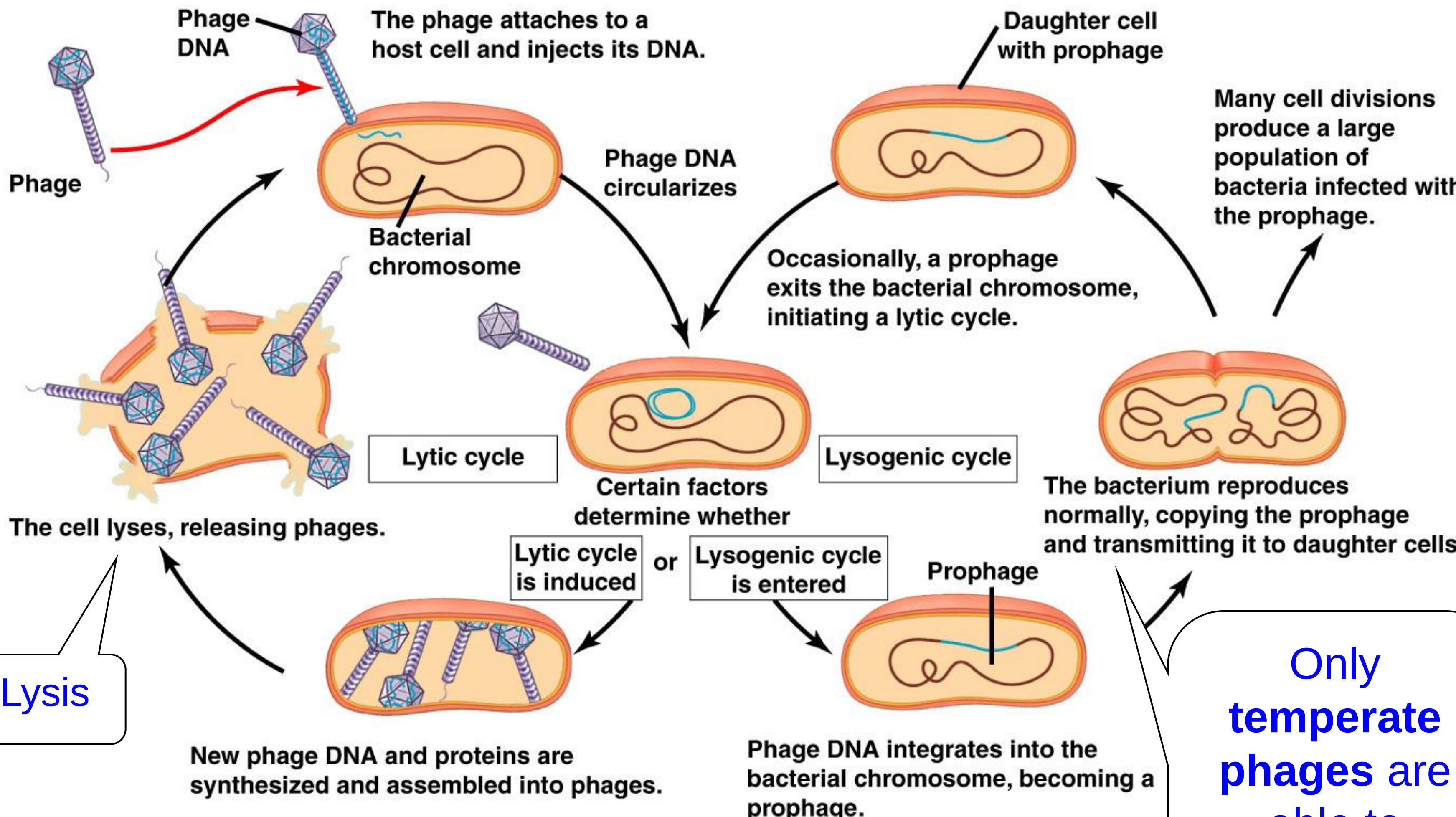
Close interactions between loci are a consequence of coevolution

These genes are nearly useless if transferred individually

Transduction and Linkage

- Temperate phages can carry genes that modify host phenotype during lysogeny
- These genes are called converting genes, as in lysogenic conversion
- To the extent that the prophage is not induced, its genes are linked with those of its host
- These genes can include nasty toxin genes including Shiga toxin (*E. coli* O157:H7), cholera toxin (*V. cholerae*), and diphtheria toxin (*C. diphtheriae*)
- Prophage and bacterial genes are not completely linked since prophages and bacteria can always go their separate ways (induction of productive infection)
- Prophages are also subject to recombination with other phages, or with DNA "snippets"
  - Prophages can both lose and gain genes
  - The latter is sex, and results in the mosaic nature of phage genomes

Lysogeny (Temperate Phage)



Lysis

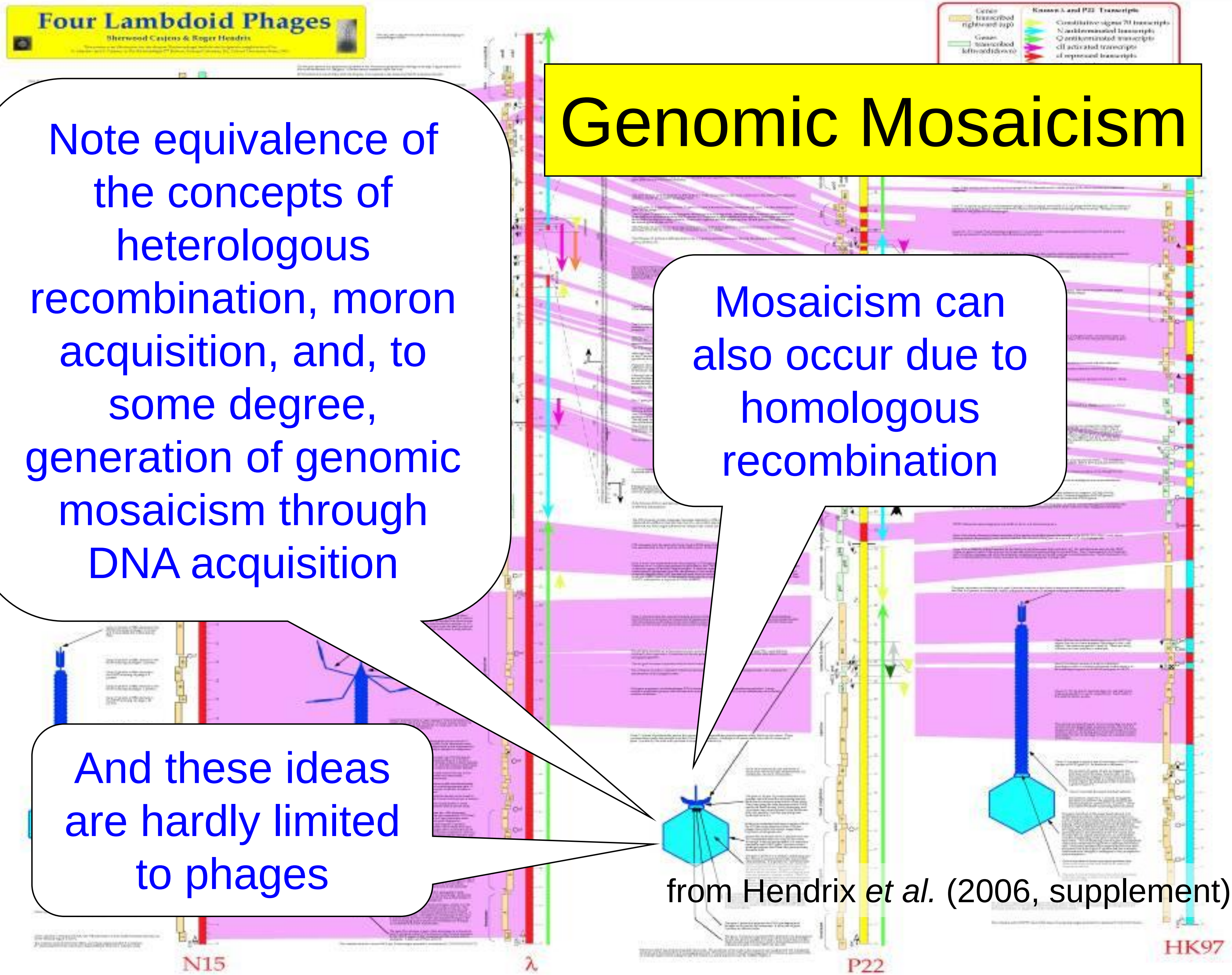
Only **temperate phages** are able to display lysogeny

Genomic Mosaicism

Note equivalence of the concepts of heterologous recombination, moron acquisition, and, to some degree, generation of genomic mosaicism through DNA acquisition

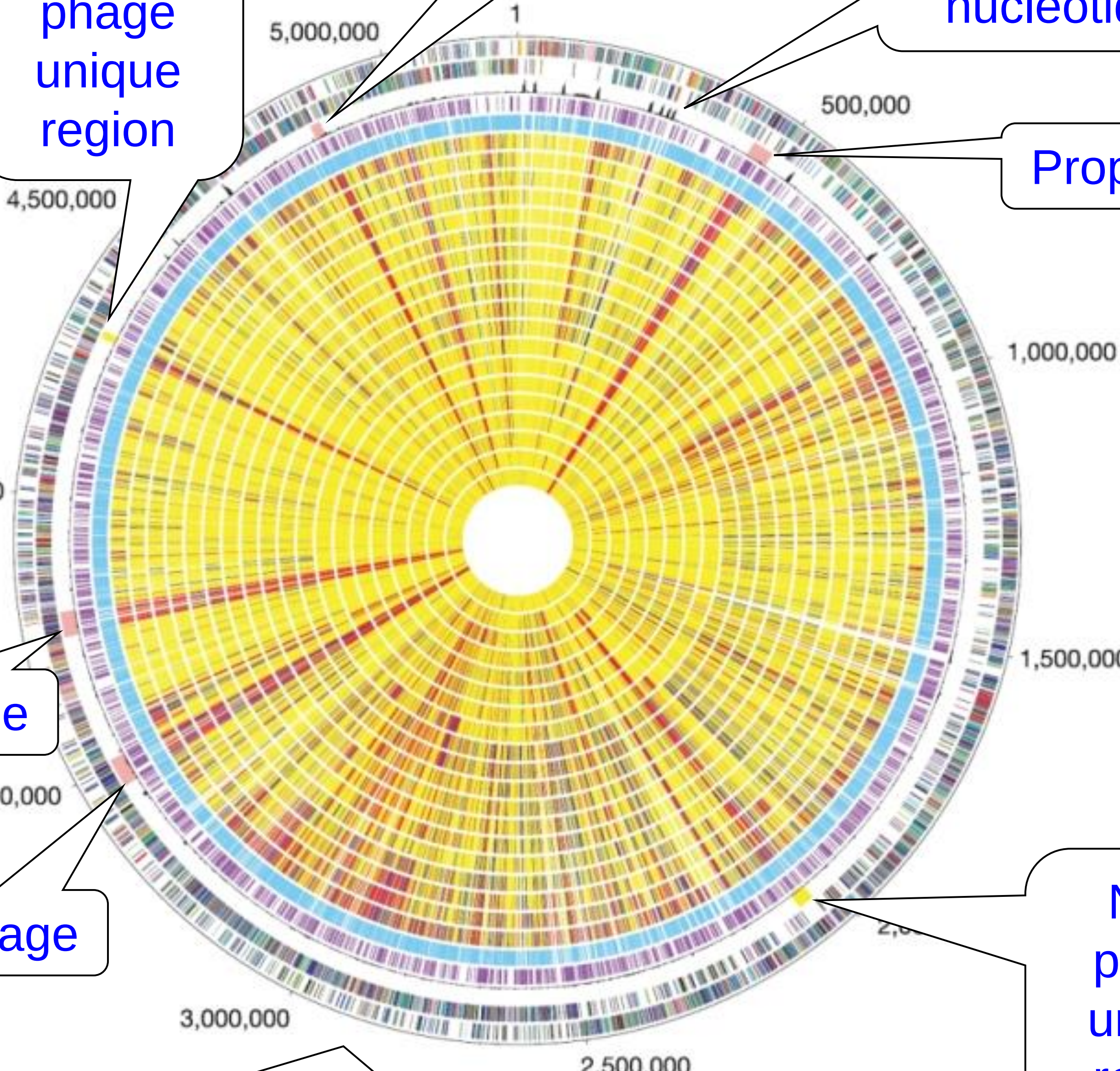
Mosaicism can also occur due to homologous recombination

And these ideas are hardly limited to phages



from Hendrix *et al.* (2006, supplement)

Bacterial Mosaicism



Non-phage unique region

Prophage

Atypical nucleotides

Prophage

Prophage

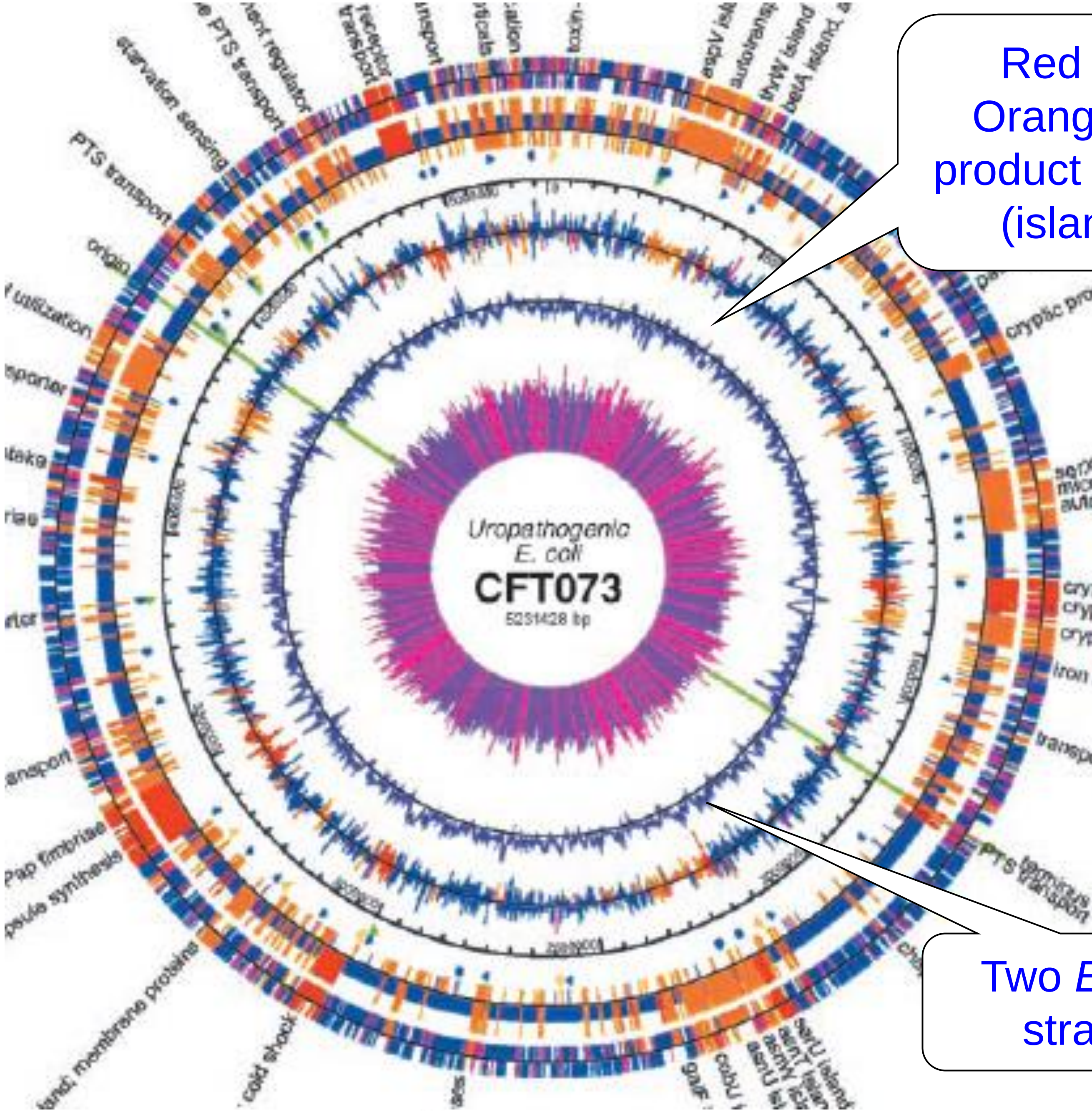
Prophage

Non-phage unique region

B. anthracis vs. *B. cereus*

Griswold (2008)

Bacterial Mosaicism



Red and Orange are product of HGT (islands)

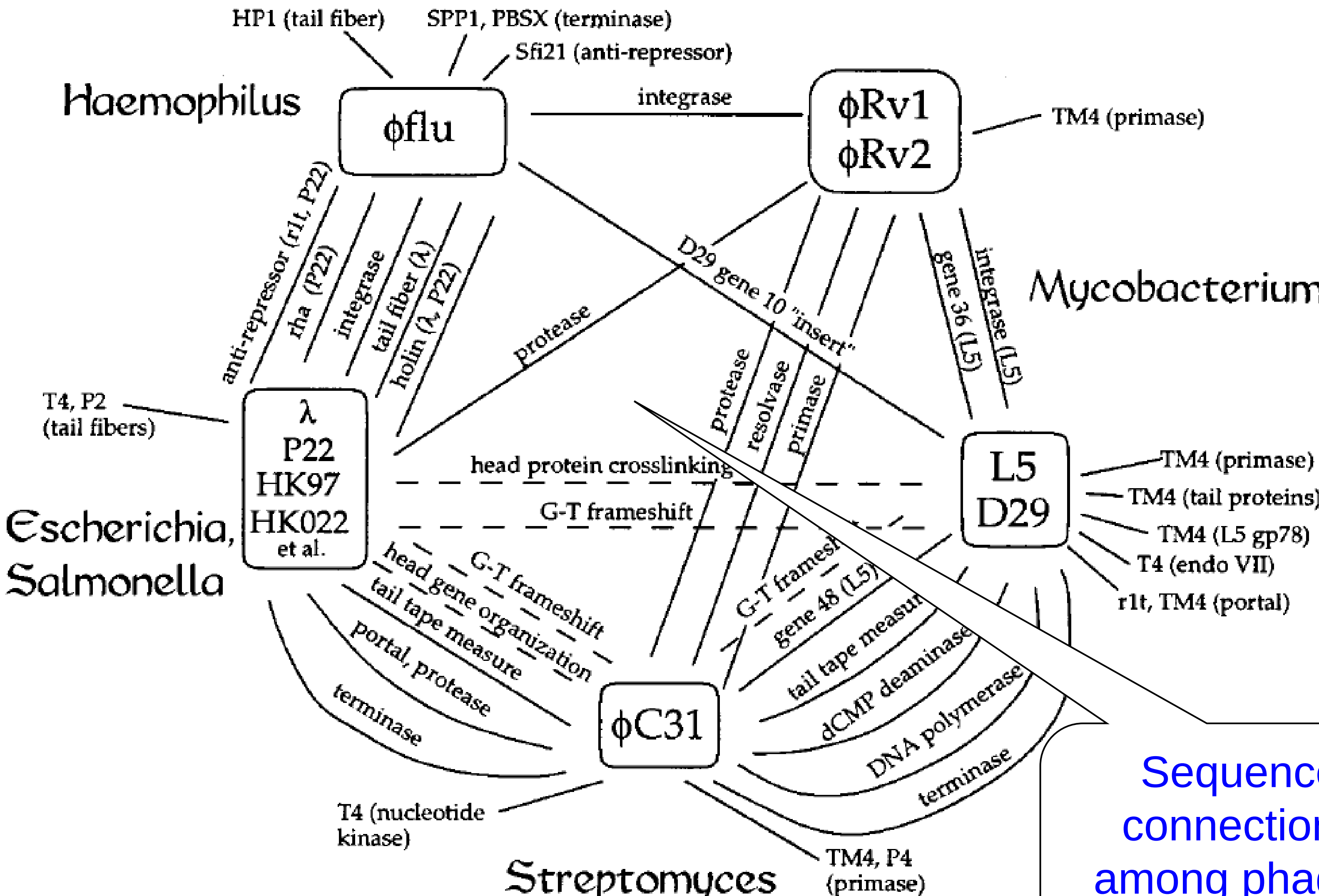
Two *E. coli* strains

Welch *et al*. (2002)

HGT + Selection = Mosaicism

- “The large number of transferred genes we find in modern bacterial genomes [mosaicism] has misled many researchers about the benefits of genetic exchange.
- “Many of the transferred genes are obviously beneficial to their new hosts and this is frequently interpreted as conclusive evidence that gene transfer must be adaptive
- “The foreign origin of many of these genes is firmly established, but the bacterial genomes that they are found in are unfortunately a very biased record of evolutionary processes.
- “The problem, of course, is natural selection.
- “Because natural selection eliminates almost all deleterious changes, the genomes of modern organisms are the result of several billion years of evolutionary success stories, with not a single failure represented.
- “In a way, the sequences we see are a type of anecdotal evidence — each represents a unique event that has, against the odds, survived.” — Redfield (2001)

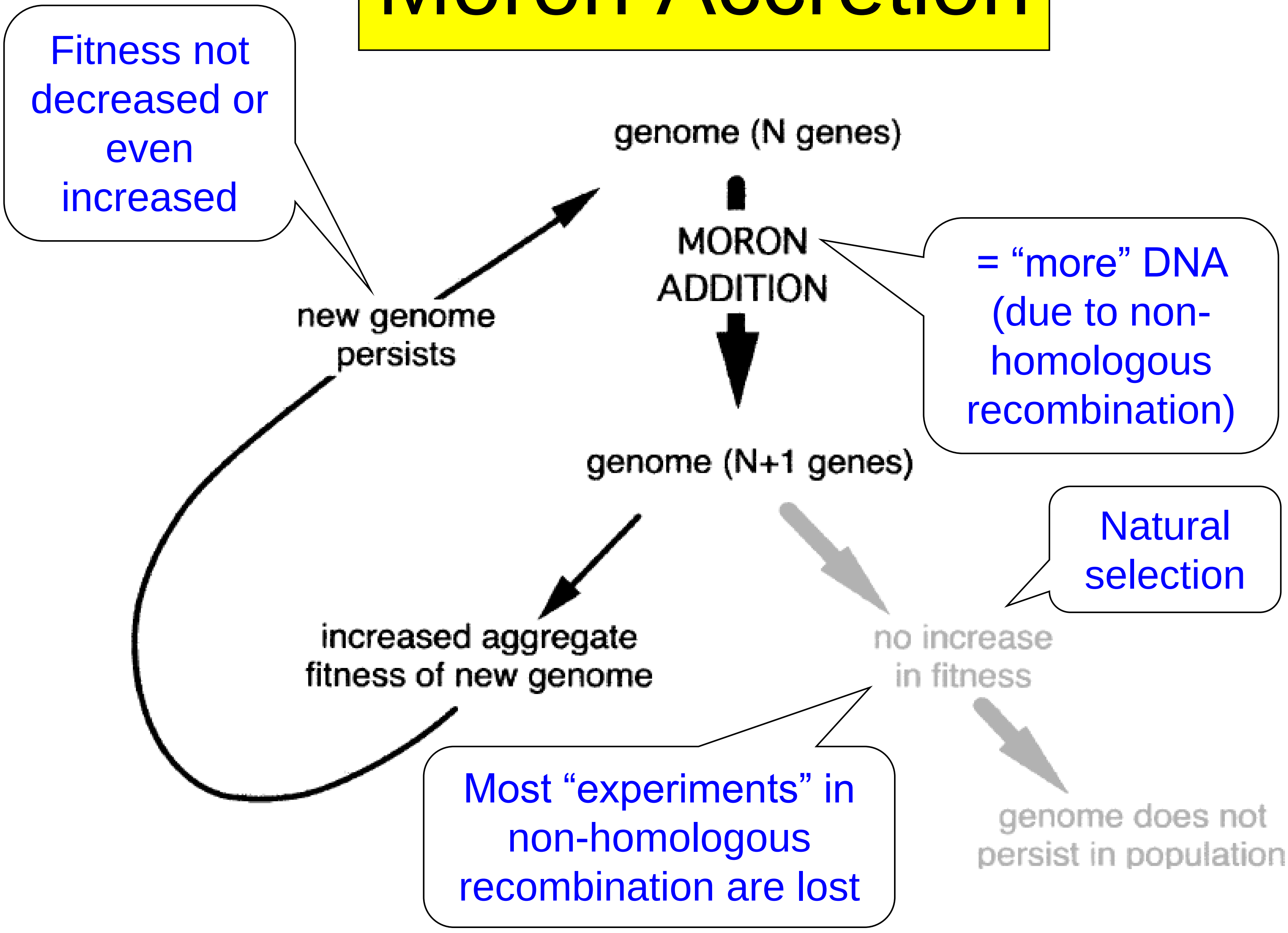
Huge Amounts of Mosaicism



Hendrix *et al.* (1999)

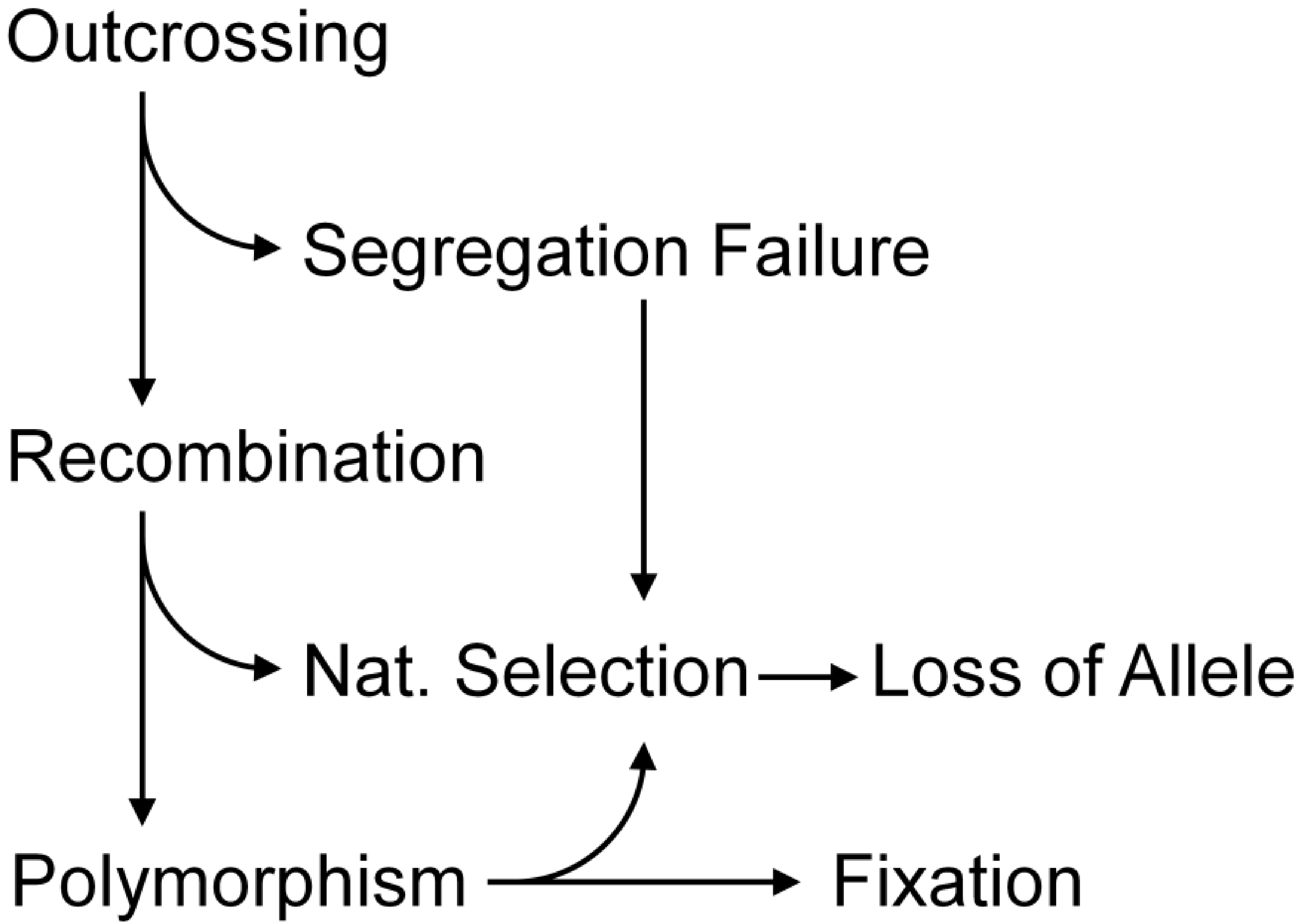
Sequence connections among phages and prophages

Moron Accretion



Hendrix *et al.* (2003)

Sex and Natrual Selection



Consequences of Sex (1/2)

1. Biological species concept (& maintenance of species cohesivity) 😐
2. Loss of genotypes (i.e., parental genotypes) which have stood the test of selection ☹
3. Breaking up epistatic interactions/linkage between coevolved genes (=segregation/recombination load; same as above but with synergy) ☹
4. Greater potential for within-genome disharmony ☹
5. Breaking up epistatic interactions/linkage between coevolved parasitic genes ☺
6. Avoidance of Muller's ratchet ☺
7. Avoidance of selection-associated purging of genetic variation (i.e., periodic selection and resulting hitchhiking) ☺
8. Avoidance of clonal interference ☺

Consequences of Sex (2/2)

8. Avoidance of clonal interference ☺

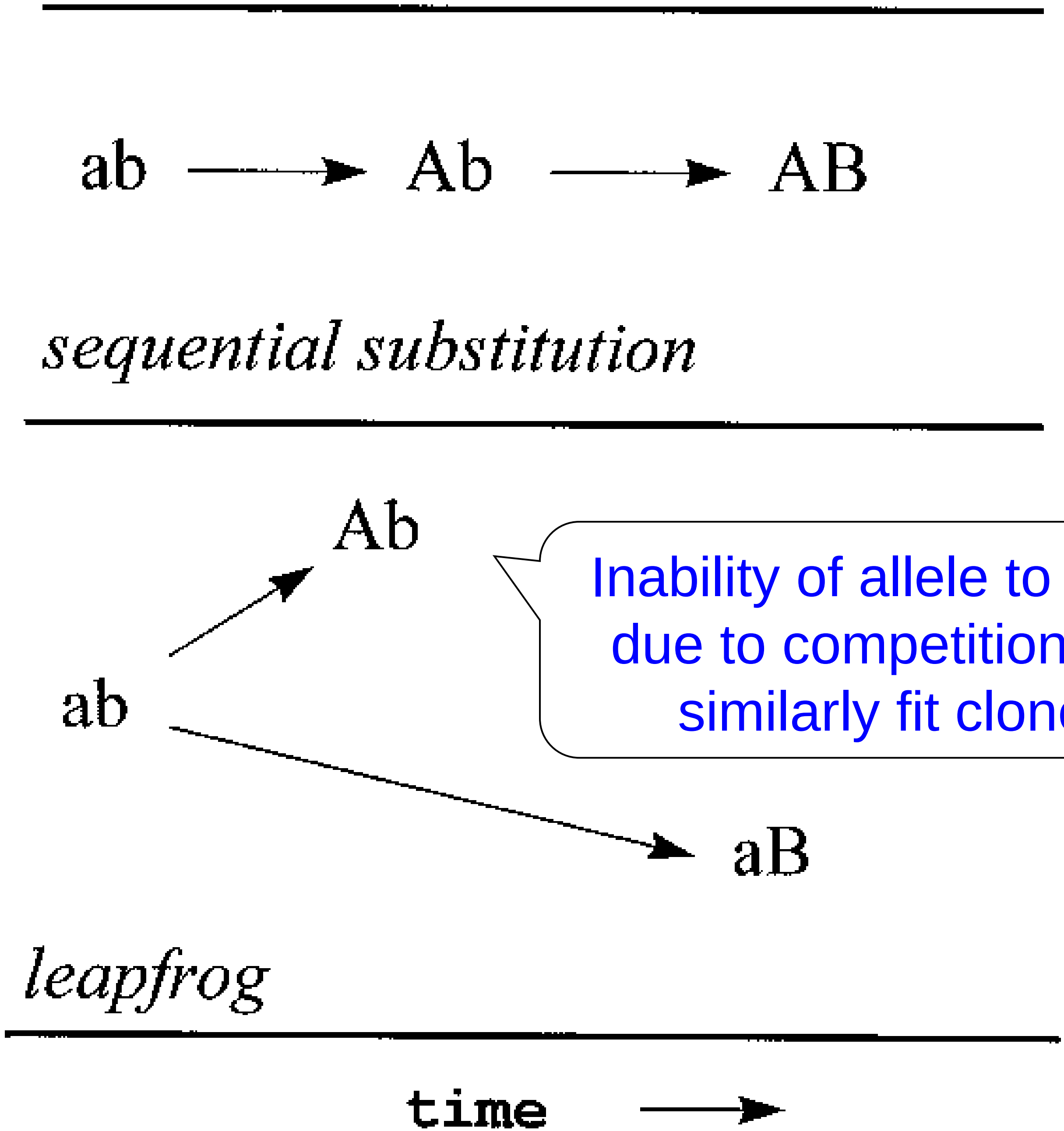
9. Increase in the amount of variability in individuals ☺:

   - Bringing together alleles originating in different lineages

   - HGT + illegitimate recombination increases amount of variability by providing bacteria with an ability to obtain novel whole genes/pathways/islands that evolved in different bacterial lineages (rapid acquisition of new traits)

10. Increase in rates of adaptation resulting from increased genotypic variation ☺

Clonal Interference



Inability of allele to thrive due to competition with similarly fit clones

Gerrish & Lenski, 1998

Periodic Selection

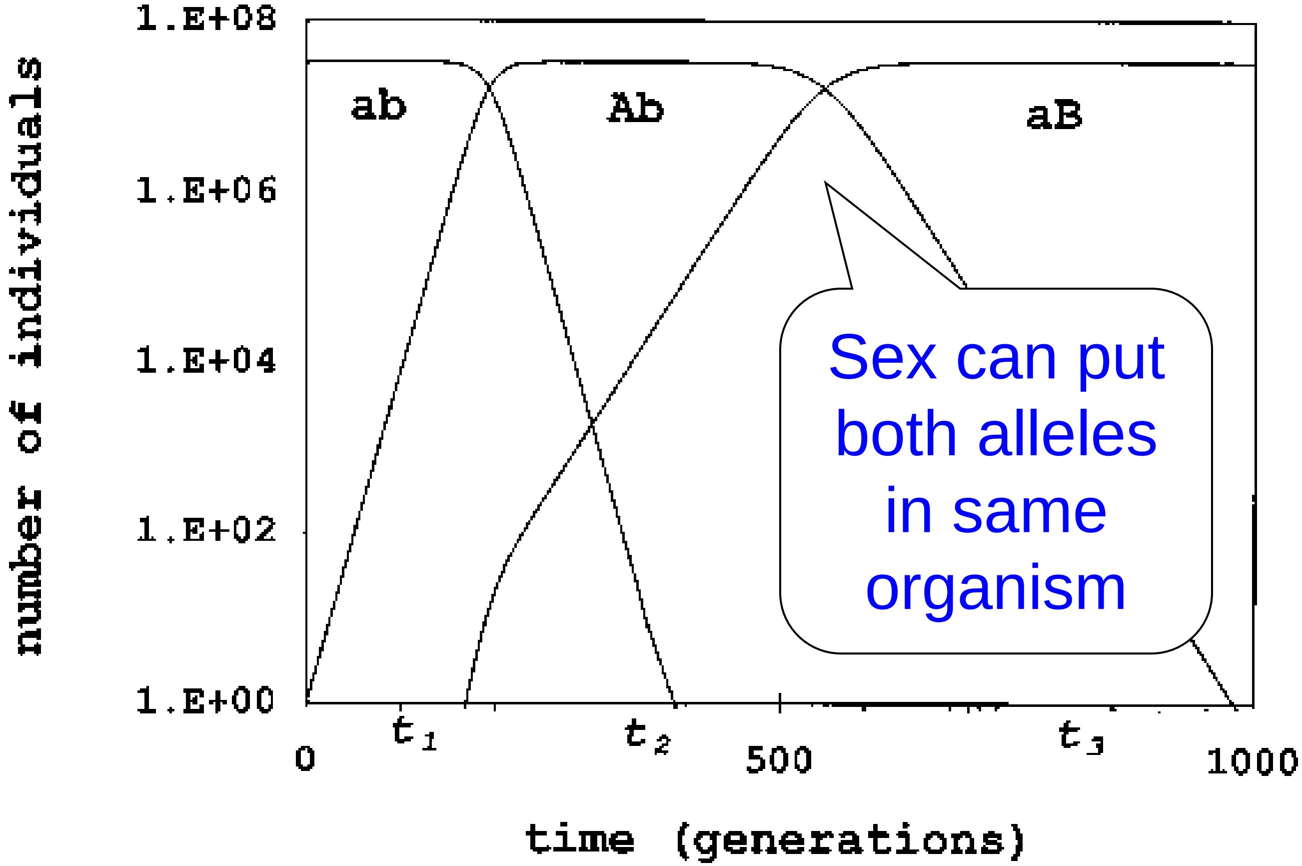


Figure 8. The leapfrog phenomenon illustrated dynamically. Genotype *ab* is displaced by mutant *Ab*, which is later displaced by alternative mutant *aB*. Equations (25) and (26) with $s_y = 0.09$, $s_z = 0.13$. Note that genotypes sampled at time t_3 are more closely related to those sampled at t_1 than to those sampled at t_2.

Gerrish & Lenski, 1998

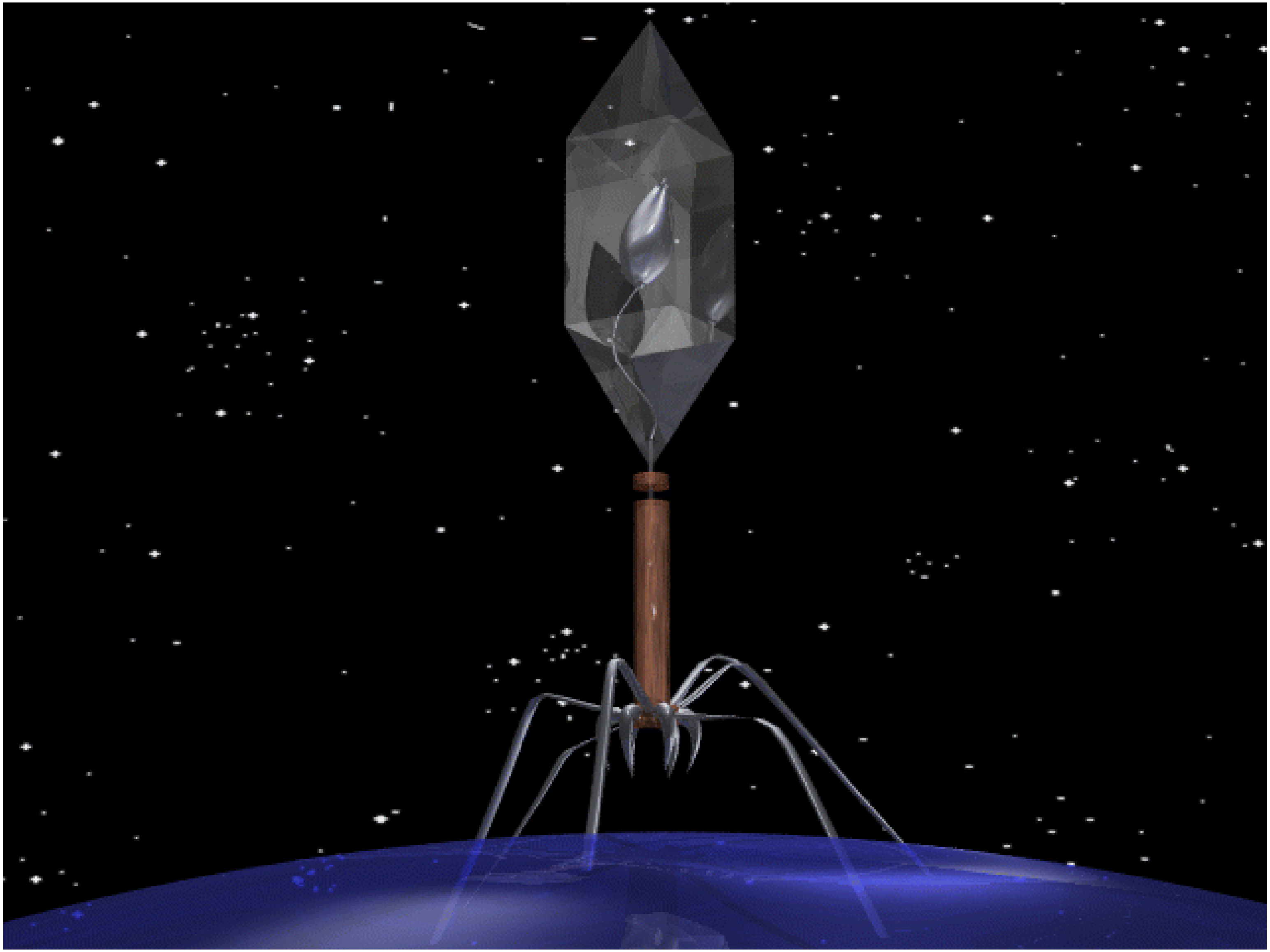
Why Bactreria Have Sex

- Bacteria are much more promiscuous than eukaryotes, at least in the sense of what kinds of individuals they are "willing" to have "sex" with
- Bacterial mechanisms of recombination likely exist as means of non-error-prone DNA repair (i.e., repair of DNA damages in a manner that does not result in mutation)
- Bacteria outcrossing usually does not appear to be a function of bacterial adaptations
  - Or if a consequence of bacterial adaptations then not necessary adaptations that exist specifically to enhance outcrossing (e.g., transformation as food acquisition)
- Bacteria, over longer time scales, can benefit from DNA movement between different bacterial species
- Advantages of horizontal gene transfer, or just sex in general, likely do not justify the maintenance of these functions in modern bacterial populations
  - But if obtaining substantial variation can justify being able to have sex, e.g., display of competence (transformation), then advantage is like that of general mutator alleles
  - Hitchhiking of sex alleles with acquired beneficial alleles

Summary

- Which of these transfer processes is most important?
  - **Transformation**: Probably quite important for naturally competent organisms
  - **Specialized transduction**: Probably important mostly if defined broadly enough to include morons
  - **Conjugation**: For a subset of functions, such as antibiotic resistance, apparently quite relevant, though seemingly more limited in its impact than generalized transduction
  - **Hfr conjugation**: Perhaps mostly a laboratory artifact?
  - **Generalized transduction**: Hugely versatile in terms of both the types and size of DNA that can be transferred, though mostly a stochastic process so perhaps much less likely to result in selective benefits than conjugation
  - **You are what you eat**: Probably similar to generalized transduction in its consequences
- The other key take home messages are that…
  1. While mechanisms by which DNA is transferred as well as retained are important, what is particularly crucial is to what extent that DNA provides a selective benefit since absent such a benefit it is unlikely to be retained within a population
  2. Linkage, in various forms, drives the evolution of cooperation

The End



Why Have Sex?

- This question encompasses issues of
  - The evolutionary origin of sex
  - The evolutionary maintenance of sex
  - Sexual vs. asexual reproduction
  - The existence of separate genders
- In terms of origins:
  - Byproduct of repair of DNA (note incorrect usage of word "mutations" in Xu, 2004, p. 776, ¶ 3)
  - Byproduct of selfish actions of parasites (e.g., phages, viruses, or self-transmissible plasmids)
  - Sex/meiosis as reduction division
  - Sex as means of increasing genetic variation
- Few people argue that sex arose for purposes of increasing the genetic variation in individuals, though this mechanism is routinely invoked as a reason for the maintenance of sex in populations

Why Use Microbes to Study Sex

- “For several reasons, microbes will become increasingly important for investigating key parameters relevant to the evolution of sex.
    - “First, most microbes can easily and cheaply be grown and maintained in large numbers.
    - “Second, they can be stored for a long time without any change in genetic and other biological characteristics.
    - “Third, many microbial species can reproduce both sexually and asexually and the degree of sexuality can be experimentally controlled.
    - “Fourth, in some species, such as the model yeast *S. cerevisiae*, the ploidy level can be manipulated, e.g., from 1*N* to 4*N*. Therefore, genetic interactions among alleles from the same or different loci can be evaluated separately and accurately.
    - “Fifth, many relevant parameters can be measured repeatedly, accurately, and relatively cheaply.
    - “Sixth, many species of viruses, prokaryotes, and eukaryotic microbes are genetically easily tractable, thus allowing detailed investigations of the molecular mechanisms responsible for the evolution of sex. ” (Xu, 2004)
- Sex, as in HGT, is a hugely important aspect of Microbe Evolution