Harmful behavior mediated by pathogens and parasites

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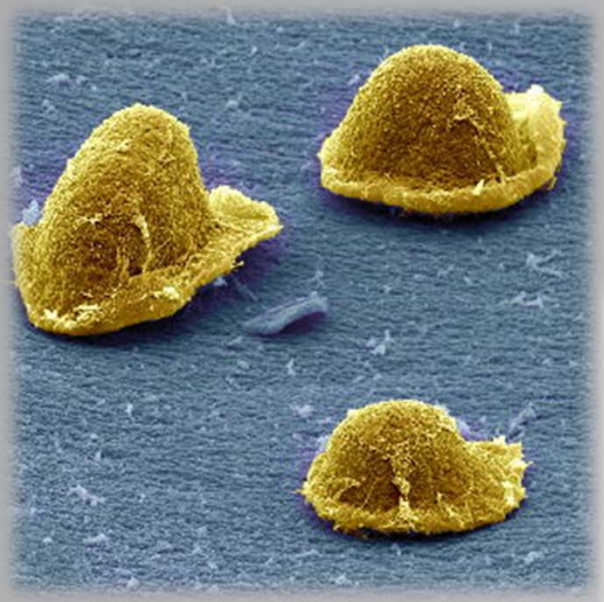
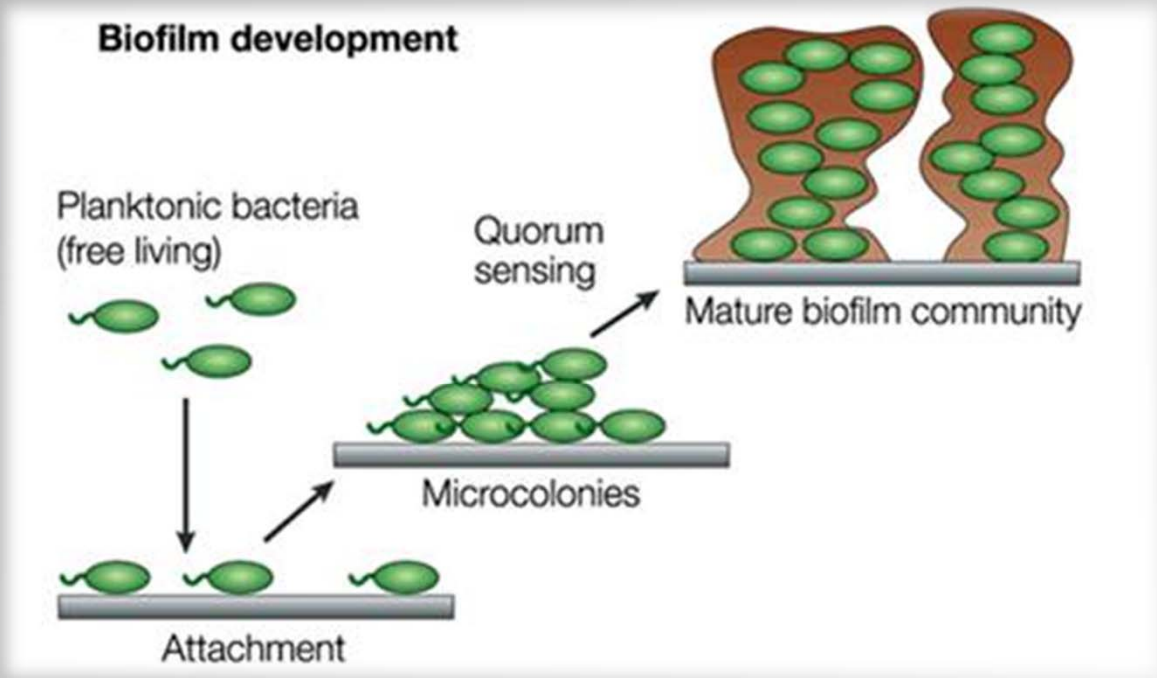
Évora, 31/January – 3/February 2017

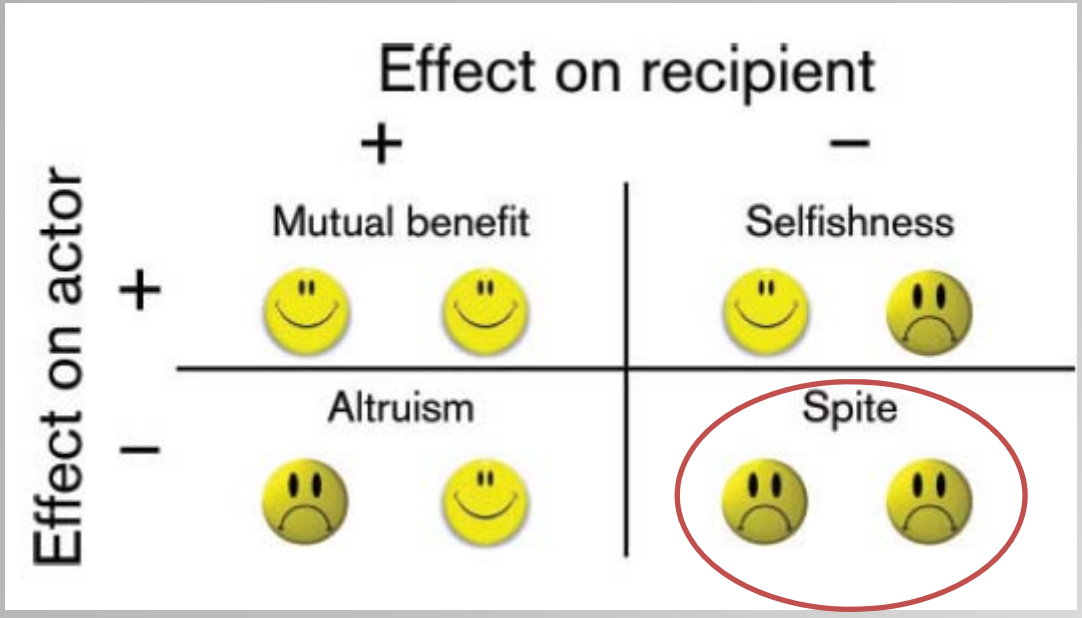
Social Behaviours

Social Behaviours in microorganisms





Social Behaviours



Clasification by W. D. Hamilton 1964, J. Theor. Biol.

- W. D. Hamilton 1964 *J. Theo. Biol*.: spite is impossible

- W. D. Hamilton 1970 *Nature*: spite is mathematically possible but biological unreasonable!

Spiteful behavior = behavior that is costly for the “actor” to be even more costly to the “recipient”.

Problems about Spite

- Spiteful actions pose a cost on the actor
- Spiteful individual has to have a way of recognizing unrelated organisms
- Populations have to be (too) small

W. D. Hamilton 1970 *Nature*

Hamilton (Nature,1970): spite is “difficult”!

- *“Of intraspecific cases it is doubtful if any can be considered confirmation of the present model.”*
- “*But why, if the model is correct, are more convincing examples of spite hard to find?*”

Spite is a behaviour that harms others without a direct benefit to the self.

From a genetic poit of view, harming non-relatives may not equal helping kin because the benefits are diluted among all the others:

kin individuals that do not pay the cost of harming non-kin individuals that are not harmed.

Spite – an exemple

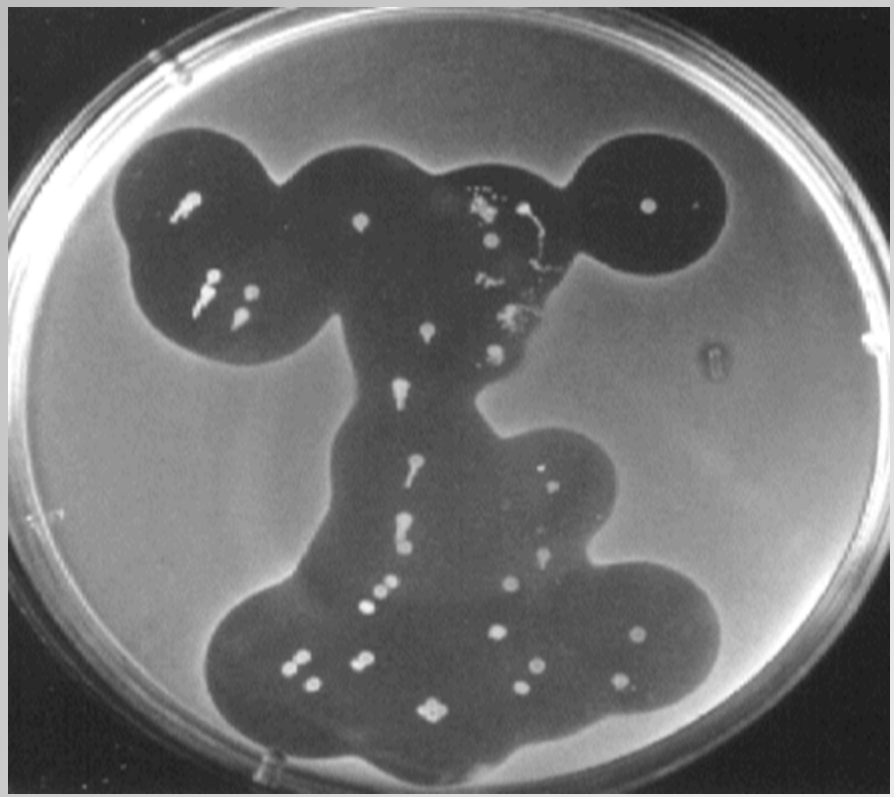
Bacteriocins

Toxins produced by bacteria to inhibit the growth of similar or closely related bacterial strains.

Production

↕

Immunity



Chao & Levin 1981 *PNAS*

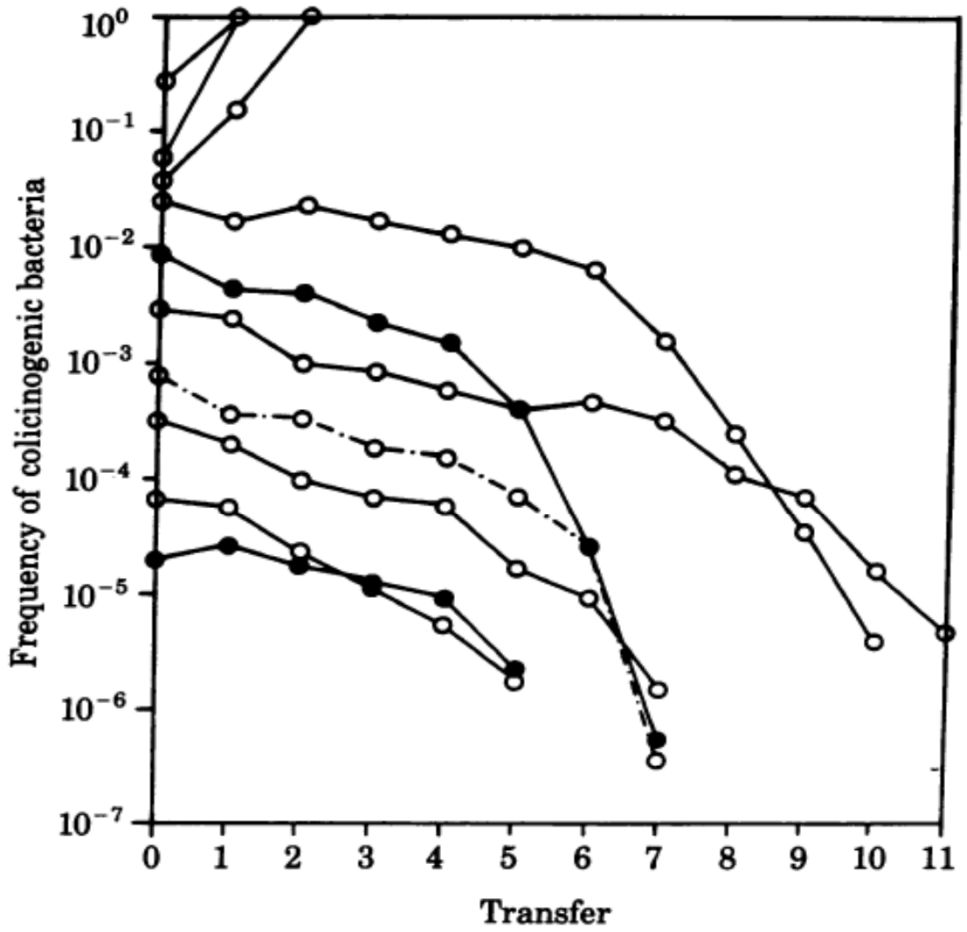
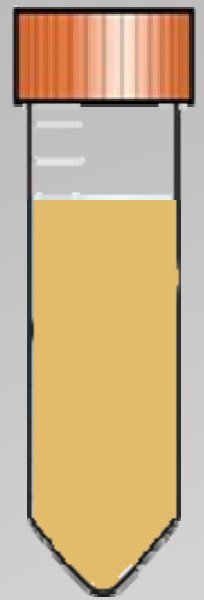


FIG. 1. Changes in frequency of colicinogenic bacteria in competition with sensitive bacteria in liquid medium cultures.



So, how can this behavior start from scratch, from a single mutant?

Chao & Levin 1981 *PNAS*

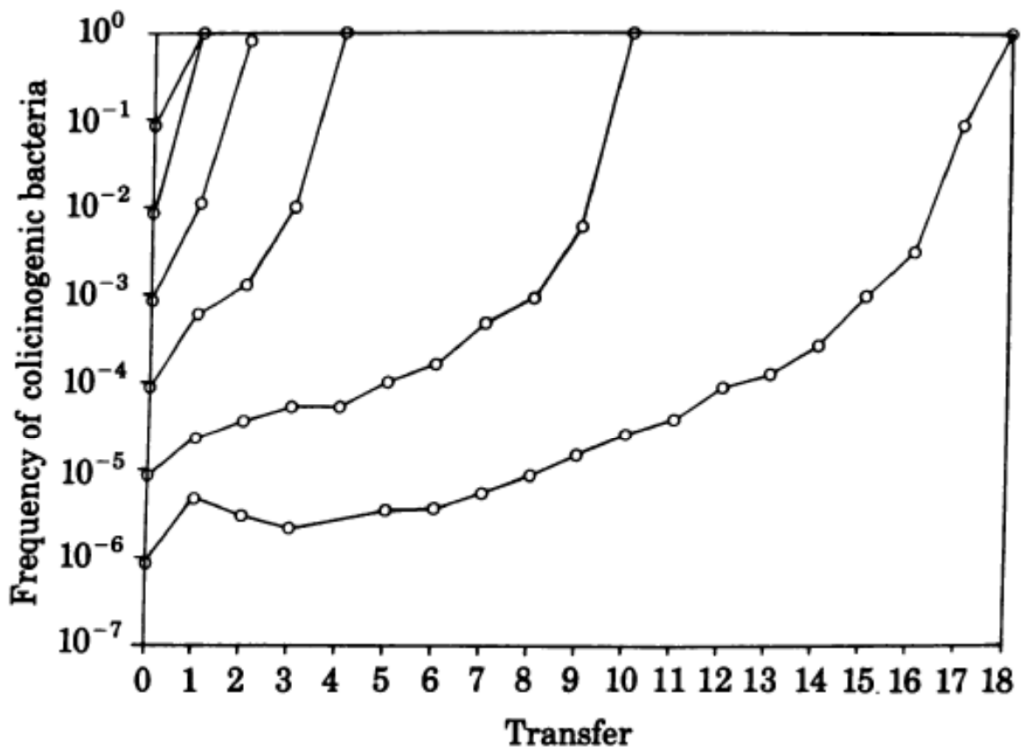


FIG. 2. Changes in frequency of colicinogenic bacteria in competition with sensitive bacteria in soft agar plates.

Chao & Levin 1981 *PNAS*

Producers of toxin

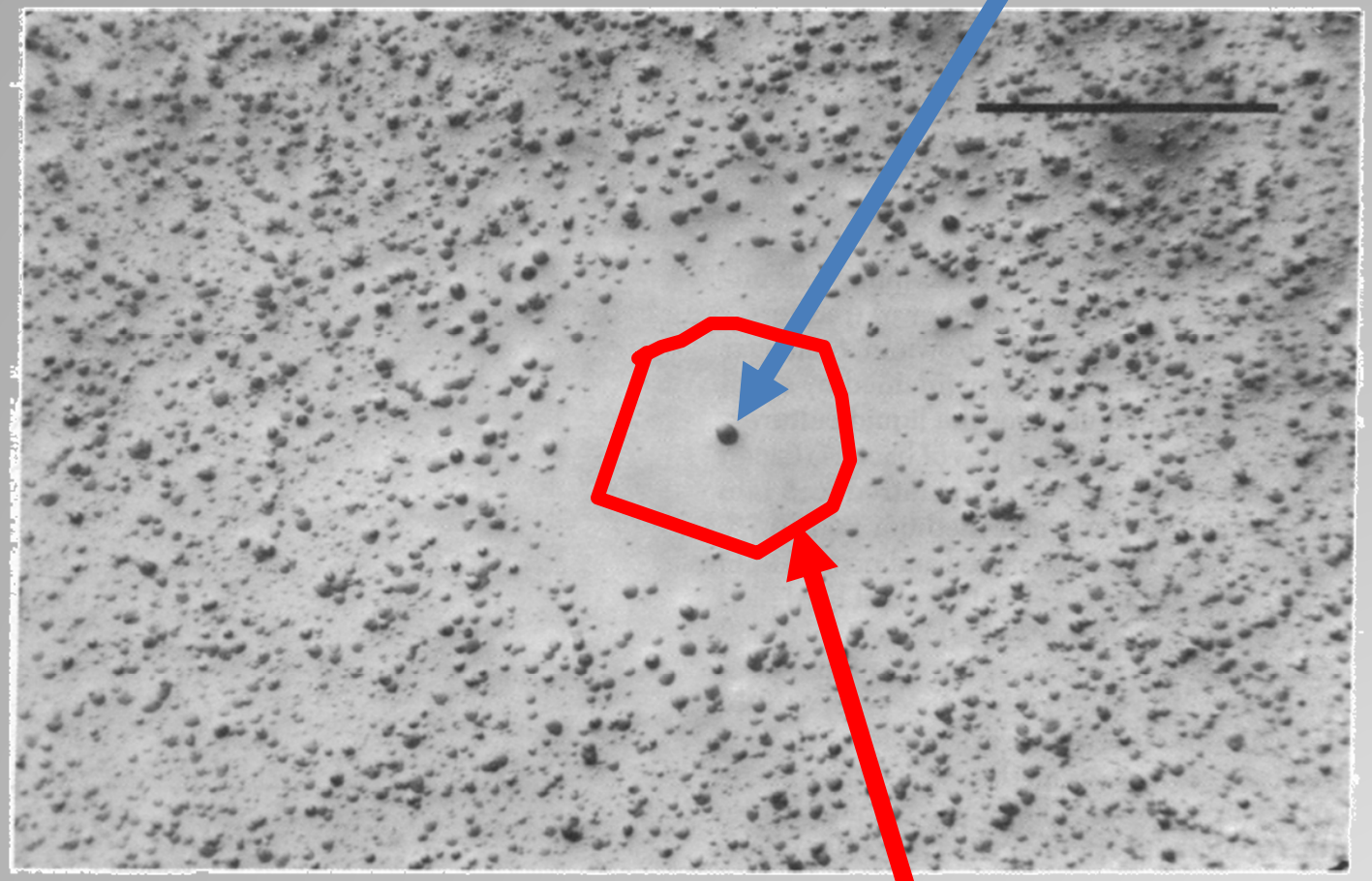
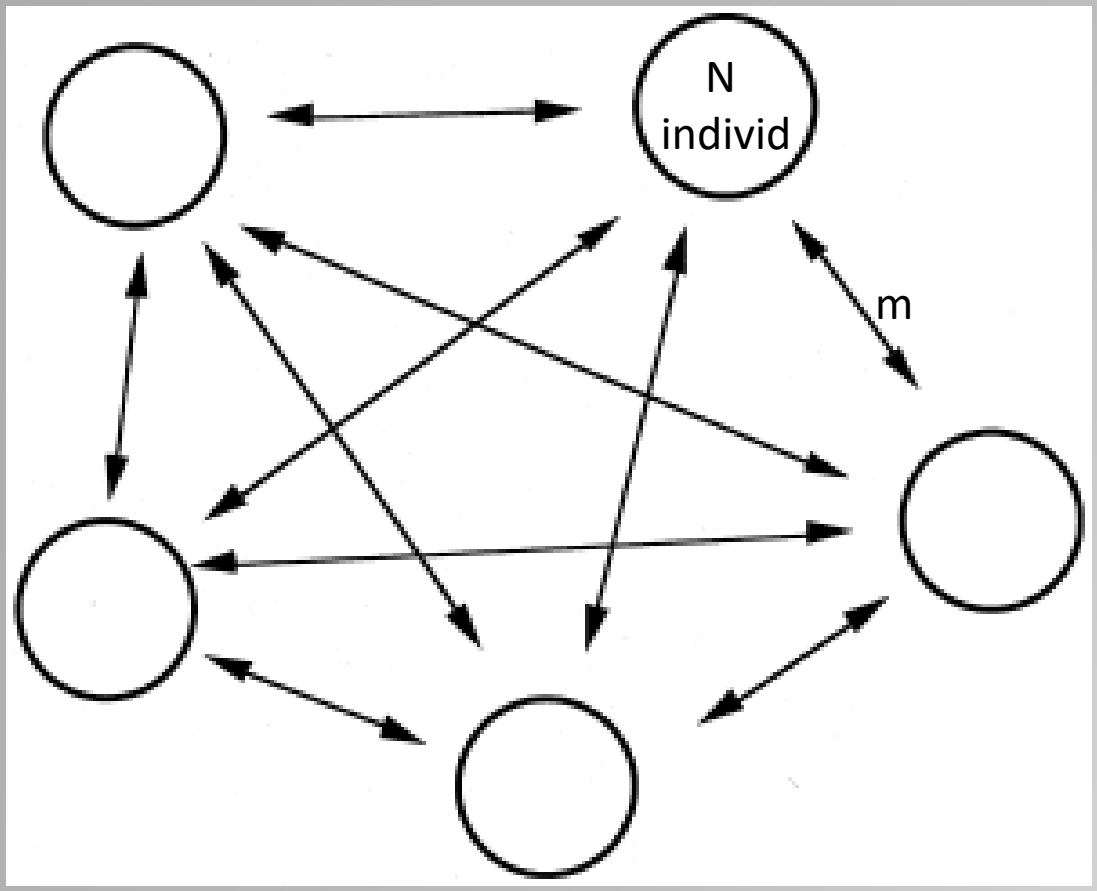


FIG. 3. Photomicrograph showing a magnified section of a soft agar plate with colonies of sensitive bacteria and one colony of colicinogenic bacteria surrounded by an inhibition zone. Scale bar equals 500 μm.

Nutrients from this zone feed the colicinogenic colony

Modelling an Infinite Island Model - Sewall Wright



Each group has N individuals

Migration rate = m

In this model, resident individuals harm incoming individuals

Cost to the spiteful individual

$$-c + b_0 + b_1 = 0$$

Effect on individuals from same deme

Effect on individuals coming from other demes

0 in the infinite island model (Wright 1943)

$$\Delta W_{F.I.} = -c.Q_{\bullet} + b_0 \cdot Q_0 + b_1.Q_1$$

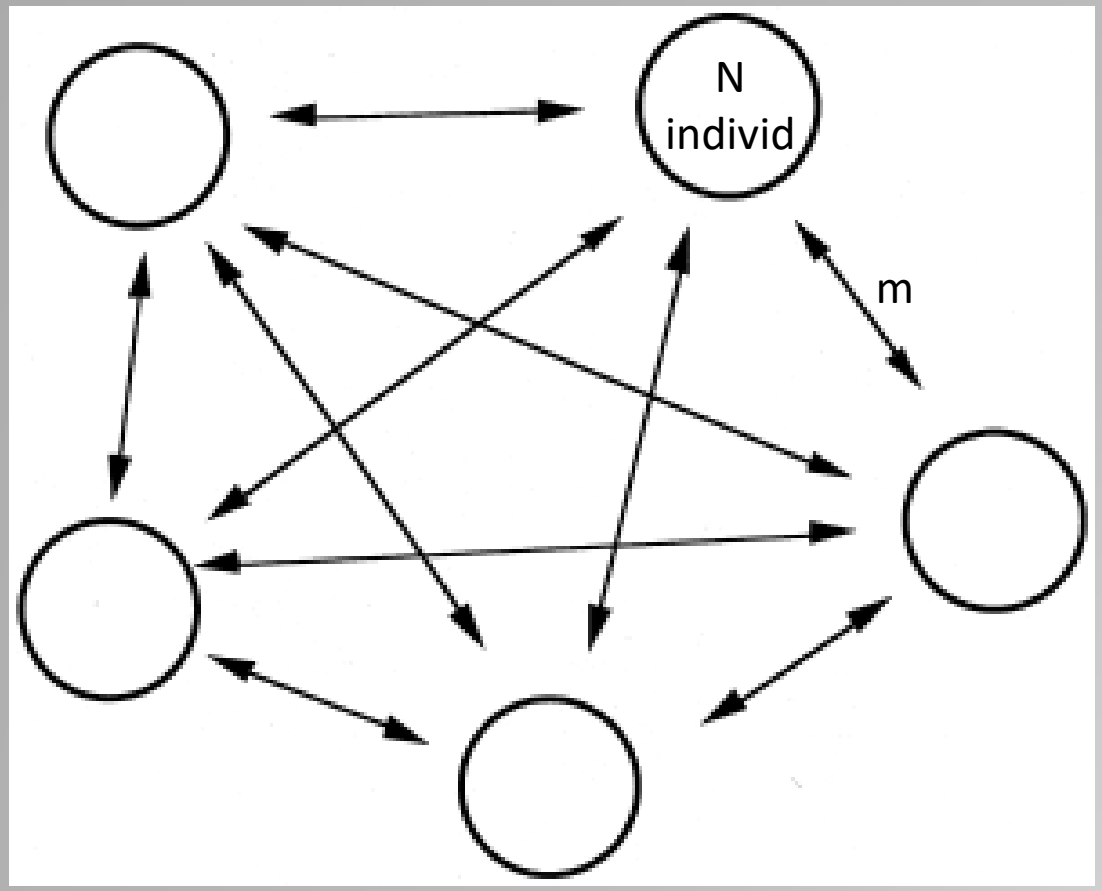
Inclusive fitness

1 or 1/2

F_{ST} for infinite island model (Wright, 1943)

F_{ST} = prob. that individuals are identic in an Infinite Island model

Infinite Island Model - Sewall Wright



Each group has N individuals
Migration rate = m

$$F = \frac{(1-m)^2}{N-(N-1)(1-m)^2}$$

Note that:

$m \to 1 \Rightarrow F \to 0$

$m \to 0 \Rightarrow F \to 1$

$m \to 1 \Rightarrow F \to 0$ If migration is intensive, individuals are diferente within each group

$m \to 0 \Rightarrow F \to 1$ That is, if there is no migration, individuals are similar within each group

Cost to the spiteful individual

$$-c + b_0 + b_1 = 0$$

Effect on individuals from same deme

Effect on individuals coming from other demes

0 in the infinite island model (Wright 1943)

$$\Delta W_{F.I.} = -c.Q_{\bullet} + b_0 \cdot Q_0 + b_1.Q_1$$

Inclusive fitness

= 1

F_{ST} for infinite island model (Wright, 1943)

m = migration rate

$$Q_0 = F_{ST} = \frac{(1-m)^2}{N-(N-1)\cdot(1-m)^2}$$

F_{ST} = prob. that individuals are identic in an Infinite Island model

I use the probability of identity by descent (F_{ST}) in subpopulations relative to the total metapopulation as a measure of the progress of genetic change.

The probability of identity by descent from a previous generation (t-1) for two alleles chosen at random in generation t from within an isolated population of size N is:
1/N.
The alternative, that the two randomly chosen alleles were not identical in generation t-1 is:
1-1/N
but these alleles may actually be identical from former generations with probability F_{ST} measured at time t-1.

Thus the total probability of identity by descent in generation t is
(Let's drop the "ST" to simplify the notation):

$$F_{t+1} = \frac{1}{N} + \left(1 - \frac{1}{N}\right) F_t$$

In the island model, one assumes that migration brings in entirely unrelated genes from infinitely many other islands or from an infinitely large mainland, with probability m.

Thus, the chance that an individual in a particular generation have not immigrated is $(1-m)$, and the probability that neither of the two individuals chosen have immigrated in that generation is $(1-m)^2$

Thus, after accounting for immigration, the overall probability of identity by descent at time t is:

$$F_{t+1} = \left(\frac{1}{N} + \left(1 - \frac{1}{N}\right) F_t\right)(1-m)^2$$

At equilibrium, F_{t+1}= F_t = F, implying that:

$$F = \frac{(1-m)^2}{N - (N-1)(1-m)^2}$$

Note that:

$m \to 1 \Rightarrow F \to 0$ If migration is intensive, individuals are diferente within each group

$m \to 0 \Rightarrow F \to 1$ That is, if there is no migration, individuals are similar within each group

Life cycle:

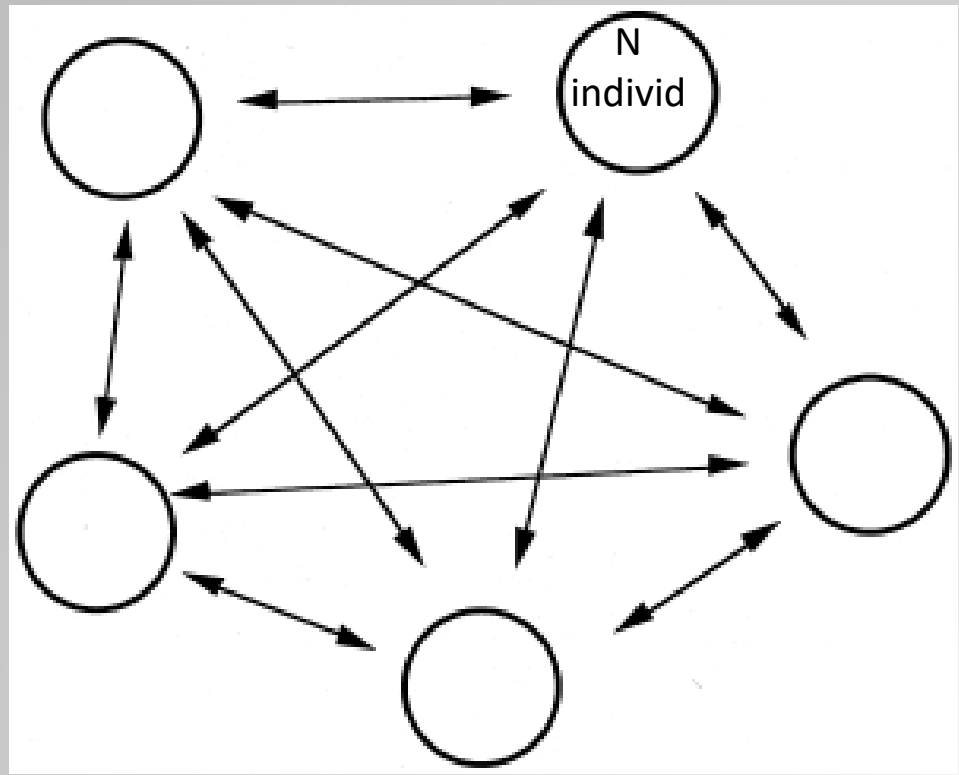
1 - each deme has *N* adults. All *N* adults breed and generate a very large number of offspring; all adults die.

2 - a fraction *m* of progeny migrates towards a random deme.

3 - offspring bearing the allele for damage **<u>harm</u> incoming offspring**.

4 - in each deme, non-migrant and immigrant individuals compete for the *N* breeding spots.

Then, the cycle begins again with the first step.



1 – T offspring. T/N descendants from the focal individual

2 – m.T juveniles migrate.

After migration, in the focal deme, the situation is:

E = m.T from External parents;

F = (1-m).T/N belong to Focal parent

G = (1-m).T.(N-1)/N belong to other parents of the focal Group

3 – Spite implies that:

E is reduced to E-e

F is reduced to F-f

T is reduced to T-e-f

What happened to the fitness of ...

$$\Delta_E = \frac{E-e}{T-e-f} - \frac{E}{T} \approx \frac{E}{T} \cdot \frac{e+f}{T} - \frac{e}{T}$$

... External parents

$$\Delta_F = \frac{F-f}{T-e-f} - \frac{F}{T} \approx \frac{F}{T} \cdot \frac{e+f}{T} - \frac{f}{T}$$

... Focal parent

$$\Delta_G = \frac{G}{T-e-f} - \frac{G}{T} \approx \frac{G}{T} \cdot \frac{e+f}{T}$$

... other parents of the same Group

Now, I define C=f/T and D=e/T

$$c \equiv \Delta_F \approx C - \frac{1}{N} \cdot (1-m) \cdot (C+D)$$

$$b_0 \equiv \Delta_G \approx \frac{N-1}{N} \cdot (1-m) \cdot (C+D)$$

F_{ST} for infinite island model (Wright 1943)

$$\Delta W_{F.I.} = -c.Q_{\bullet} + b_0 \cdot Q_0 + b_1.0 > 0$$

$$Q_0 = F_{ST} = \frac{(1-m)^2}{N-(N-1)\cdot(1-m)^2}$$

The result is that harm can be select if N< something

$$N < \frac{D}{C} \cdot \frac{(1-m)^2}{(2-m) \cdot m}$$

Exemple: If D/C=2, and m=0.1, this equation says that N<9

Therefore, this behaviour might be impossible to occur in nature

What if the harming weapon is a virus that infects 100 individuals, each one infecting other 100 individuals?

In this case, D/C=10 000!!!

$$N < \frac{D}{C} \cdot \frac{(1-m)^2}{(2-m) \cdot m}$$

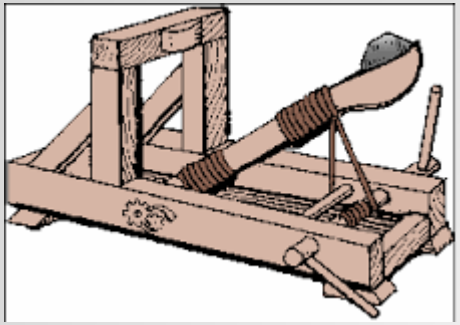
Exemple: If **D/C = 10 000**, then N < 45 000

Therefore, perhaps hosts can use parasites as “biological warfare” to fight against conspecific hosts

Any examples?

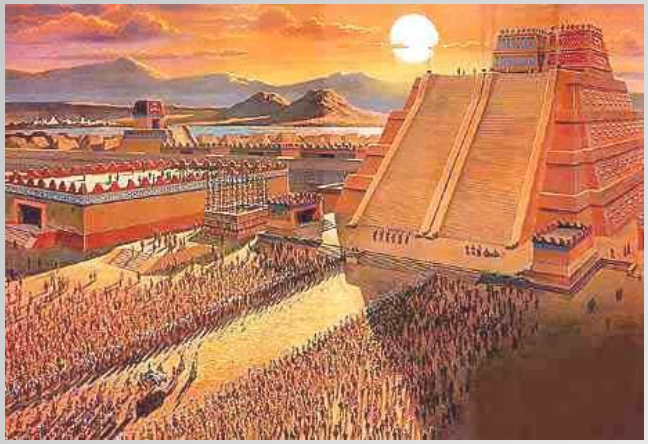
Wikipedia!

During the Middle Ages, victims of the **bubonic plague** were used for biological attacks, often by flinging fomites such as **infected corpses and excrement over castle walls using catapults**. In 1346, during the siege of Kafa (now Feodossia, Crimea) the attacking Tartar Forces which were subjugated by the Mongol empire under Genghis Khan, used the bodies of Mongol warriors of the Golden Horde who had died of plague, as weapons. An outbreak of plague followed and the defending forces retreated, followed by the conquest of the city by the Mongols. **It has been speculated that this operation may have been responsible for the advent of the Black Death in Europe.**



Humans use viruses against humans

- 90–95% of the native population of the New World was infected by Old World diseases (mainly smallpox since 1520).



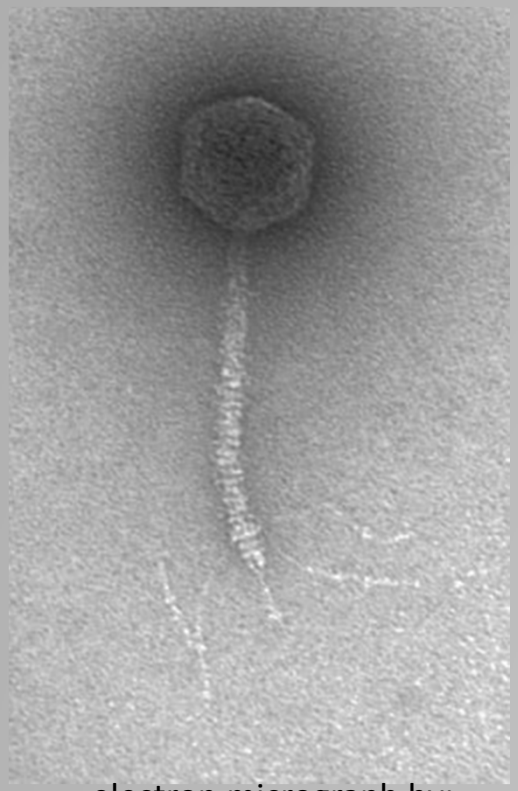
Azteca empire

Humans use bacteria against humans

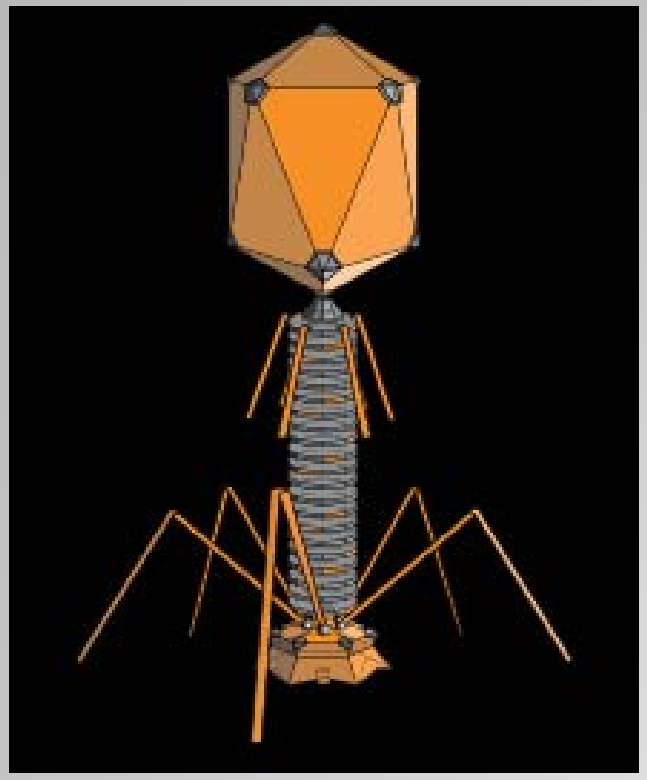
- Humans against humans: the 2001 anthrax attacks in the United States, occurred over the course of several weeks beginning on September 18, 2001.

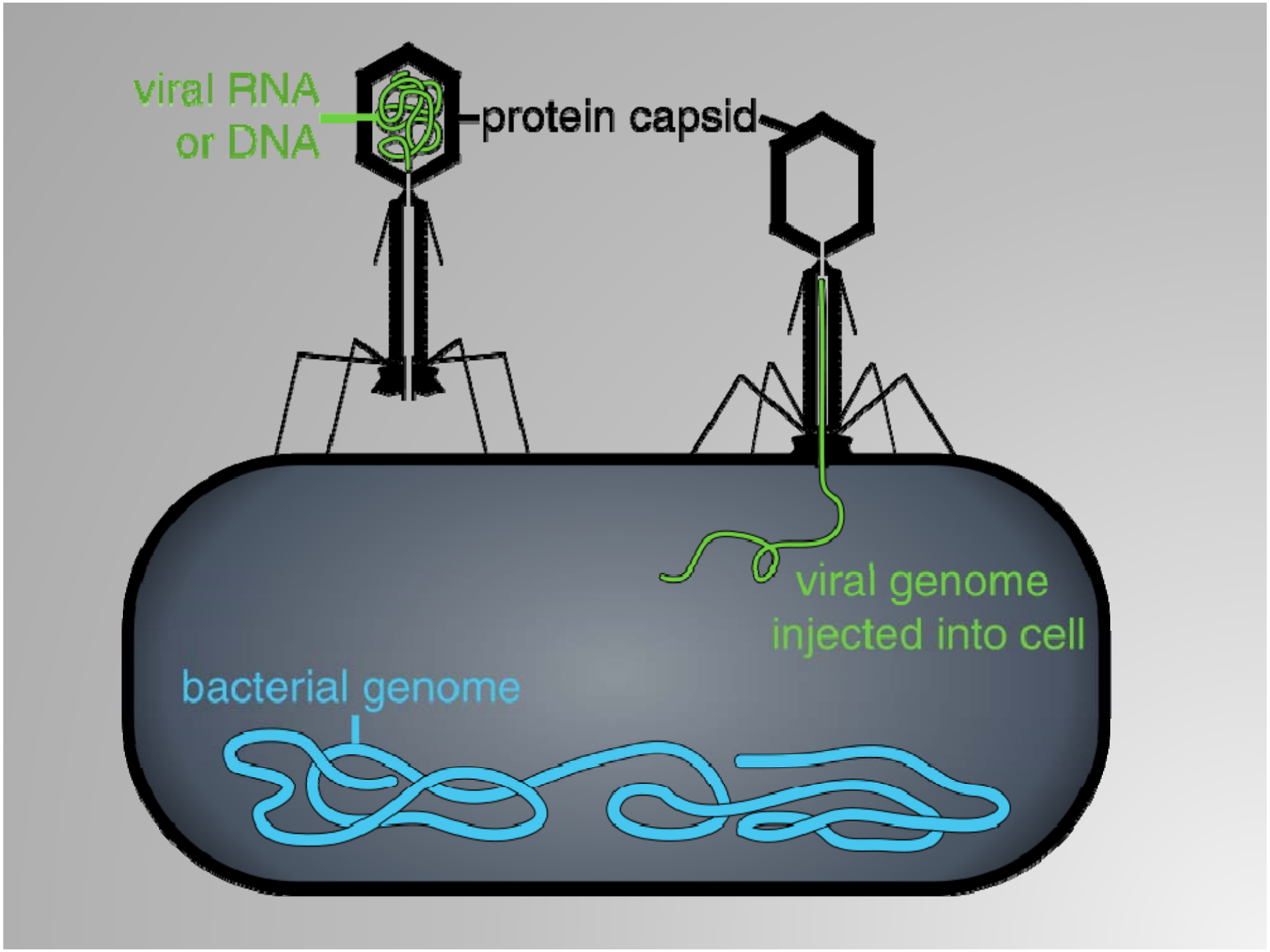
09-11-01
YOU CAN NOT STOP US.
WE HAVE THIS ANTHRAX.
YOU DIE NOW.
ARE YOU AFRAID?
DEATH TO AMERICA.
DEATH TO ISRAEL.
ALLAH IS GREAT.

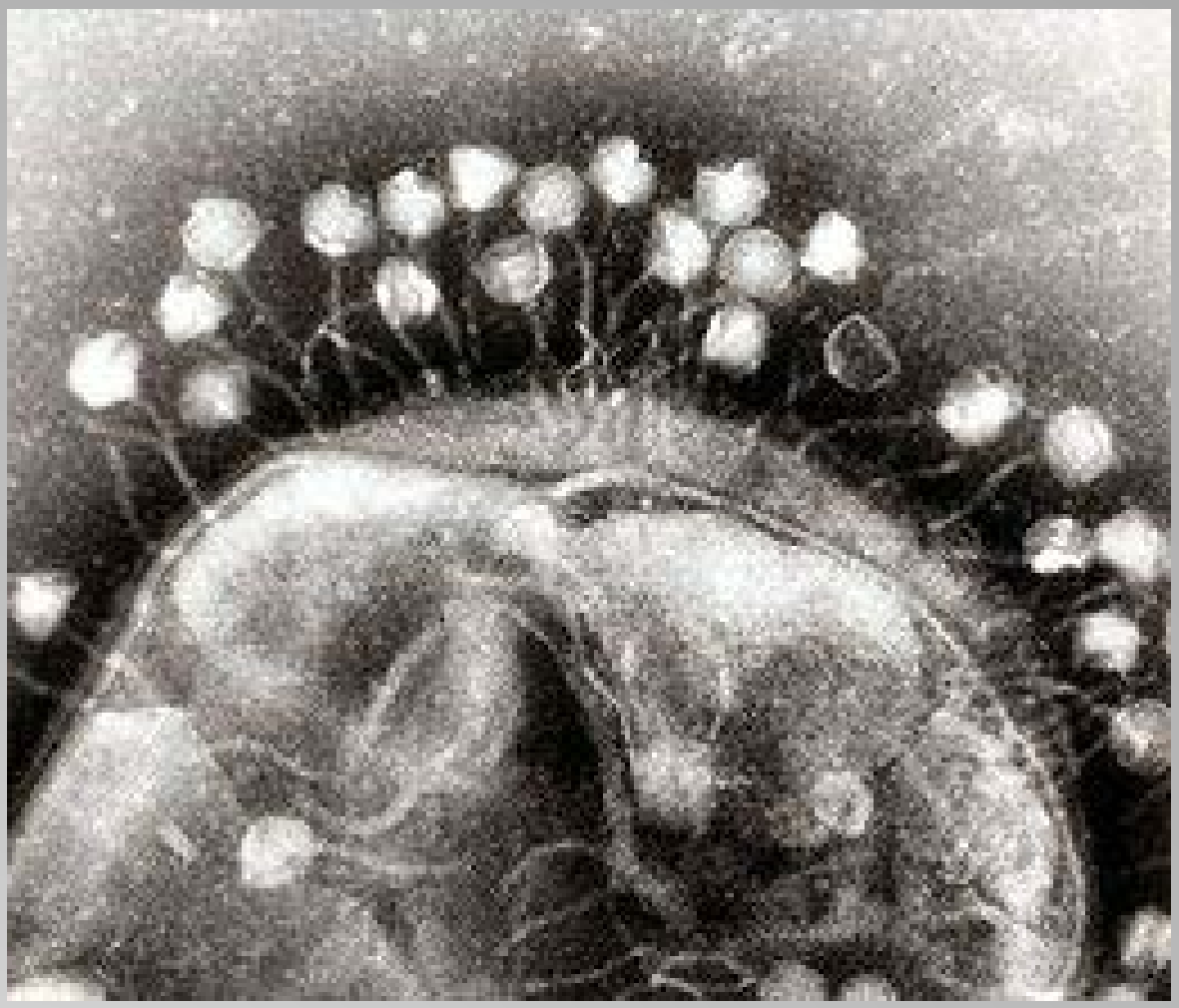
What is a bacteriophage or *phage*? It is a virus that infects bacteria.



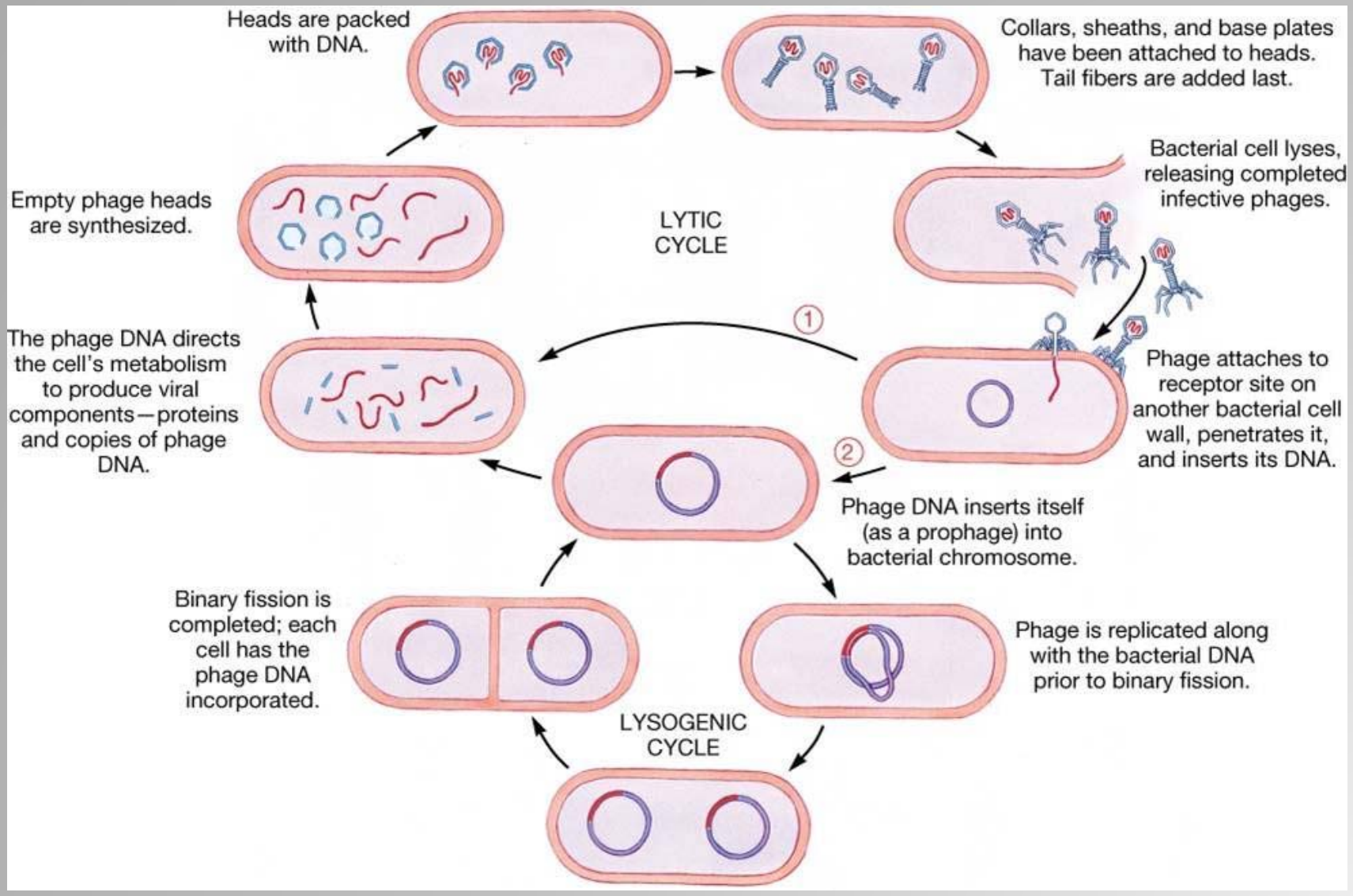
electron micrograph by:
Bob Duda (University of Pittsburgh)



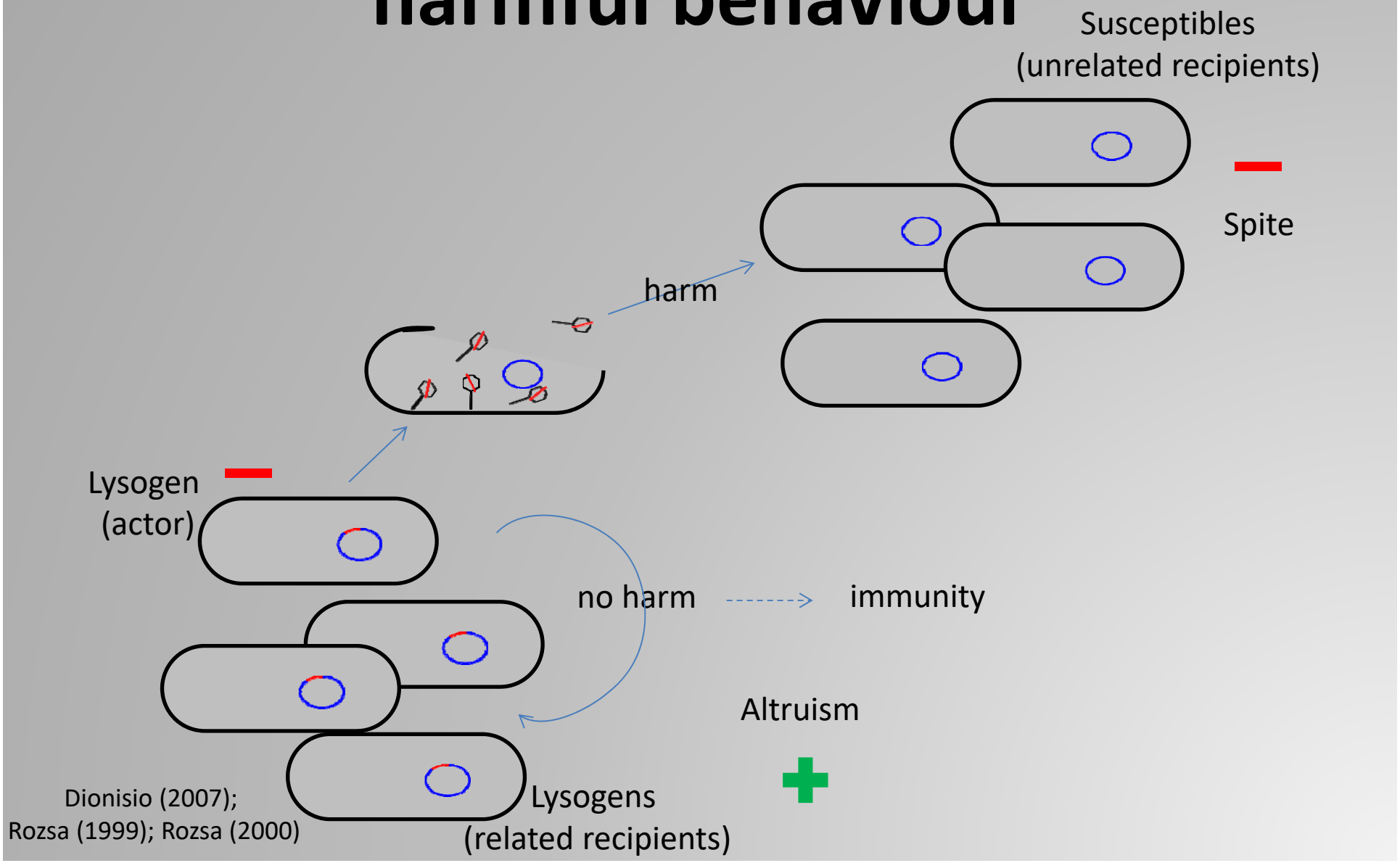

viral RNA
or DNA
protein capsid
viral genome
injected into cell
bacterial genome



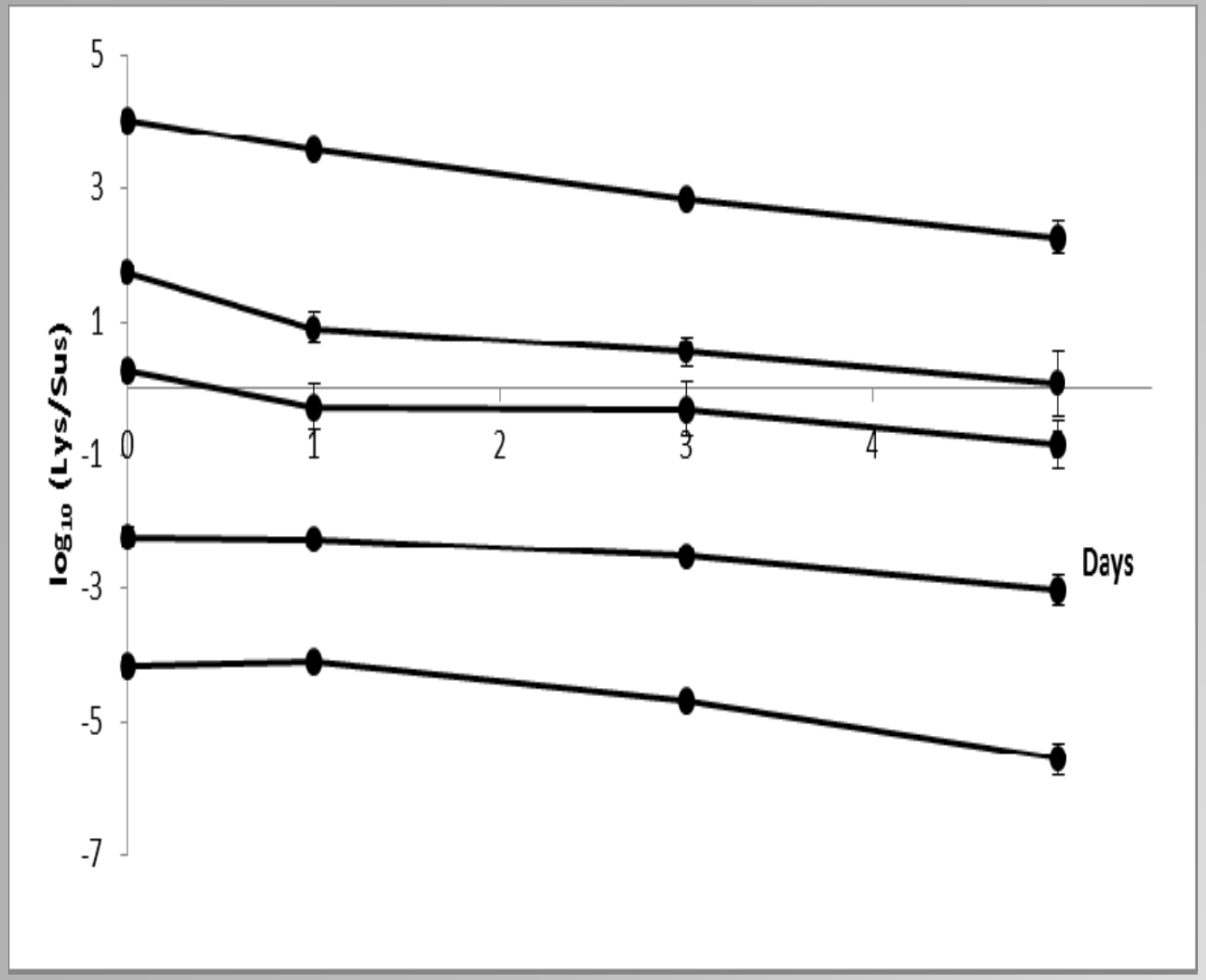
Life-cycle

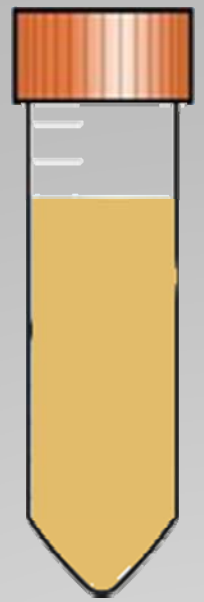

Heads are packed with DNA.
Collars, sheaths, and base plates have been attached to heads. Tail fibers are added last.
Bacterial cell lyses, releasing completed infective phages.
Empty phage heads are synthesized.
LYTIC CYCLE
1
The phage DNA directs the cell's metabolism to produce viral components—proteins and copies of phage DNA.
Phage attaches to receptor site on another bacterial cell wall, penetrates it, and inserts its DNA.
2
Phage DNA inserts itself (as a prophage) into bacterial chromosome.
Binary fission is completed; each cell has the phage DNA incorporated.
Phage is replicated along with the bacterial DNA prior to binary fission.
LYSOGENIC CYCLE

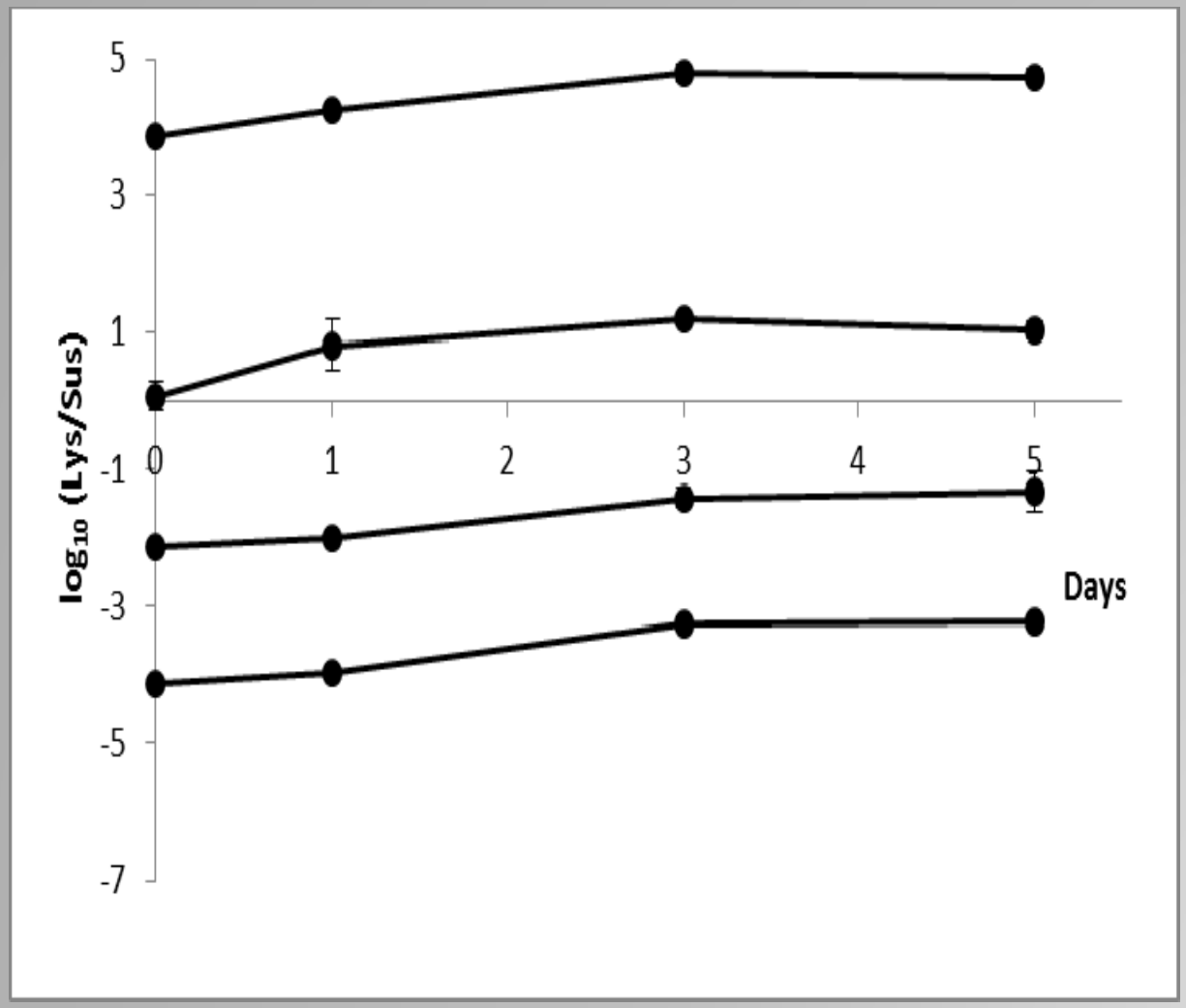
Higher competitiveness through harmful behaviour



Dionisio (2007);
Rozsa (1999); Rozsa (2000)


5
3
1
-1
-3
-5
-7
0
1
2
3
4
Days
log10 (Lys/Sus)




5
3
1
-1
-3
-5
-7
0
1
2
3
4
5
log10 (Lys/Sus)
Days

Conclusions

Unstructured Habitat → Overall Disadvantage

Unstructured Habitat → No Conversion

Structured Habitat → Advantage (short term)

Structured Habitat → Conversion (long term)

Conclusions of experiments

Bacterial cells may use bacteriophages as replicating toxins.

But they are *not* trustworthy weapons

Dionisio, F. (2007). **Selfish and spiteful behaviour through parasites and pathogens**. *Evolutionary Ecology Research* 9: 1199-1210

Biological Contribuition

Opinion TRENDS in Microbiology Vol.9 No.10 October 2001

Diversification of *Escherichia coli* genomes: are bacteriophages the major contributors?

Makoto Ohnishi, Ken Kurokawa and Tetsuya Hayashi

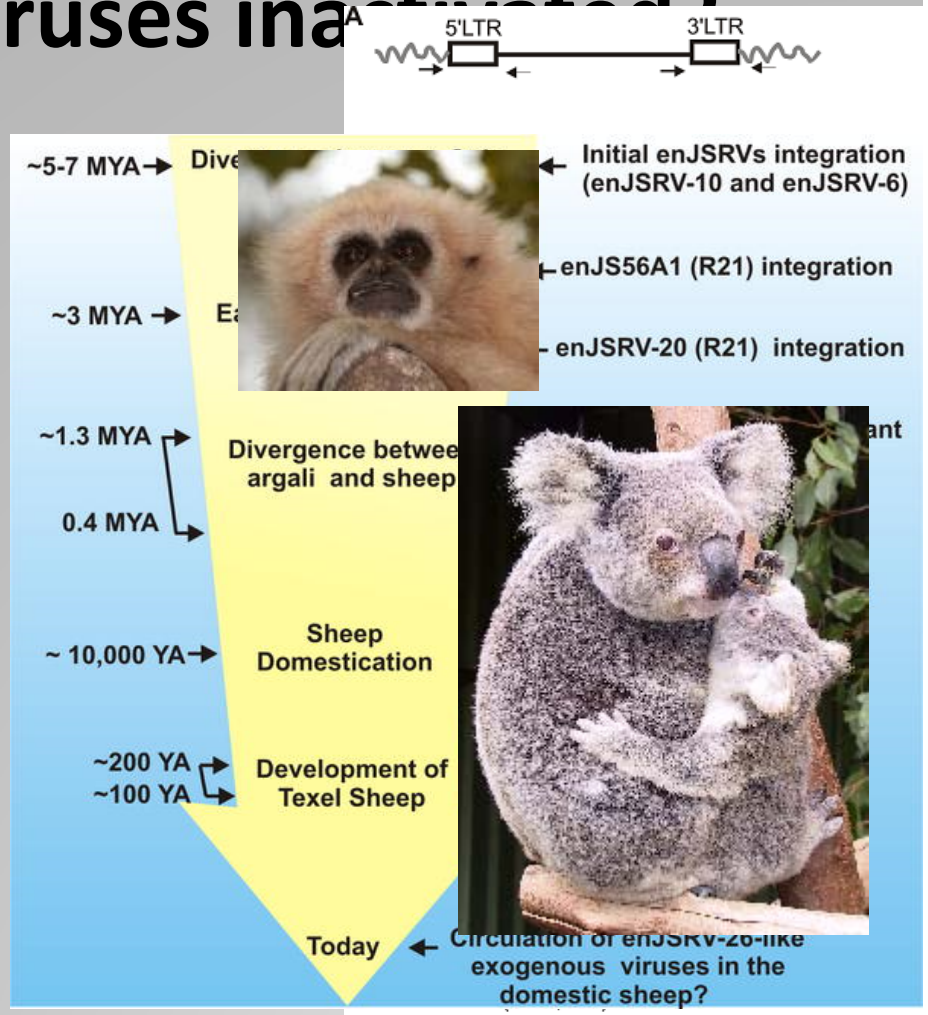
Where should we look for?

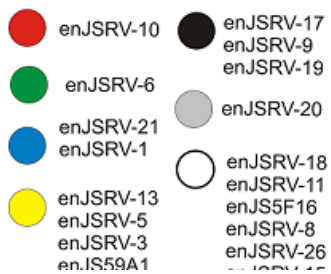
- **Endogenous Retroviruses. Examples? Some retroviruses are the cause of cancer.**

- **Humans thousands endogenous retroviruses in their chromosomes!**

Endogenous Retroviruses inactivated?

- No so fast! Examples?
- Sheep: detected virus-host coevolution sequential counter adaptation between endogenous and exogenous retroviruses (Arnaud et al. *PLOS Pathogens* 2007). Las event: around 200 years ago only!
- Humans have very recent polymorphisms of some ERV (Moyes et al *Trends in Genetics* 2007)





Why not observed before?

- Because it is also the interest of the pathogens & parasites
- How to distinguish the evolutionary interests of pathogens & parasites from that of hosts?
- Specific experiments to distinguish them have to be done.

Conclusions

- Conditions for hosts to use their pathogenes & parasites as biological weapons are very general
- Spiteful behaviour can, in fact, be much more common than expected
- If infected hosts collaborate to parasite transmission, this may have serious consequences for the epidemiology of several diseases, as it may profoundly affect estimates of disease transmission.
- This may be particularly relevant for the cases of cancers caused by retroviruses.

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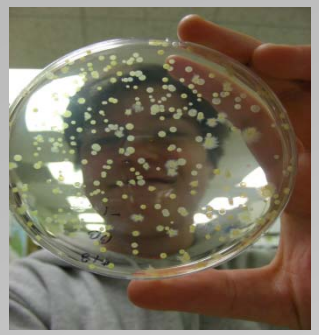

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