

Horizontal gene transfer, influence on evolvability

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Overview

- What is horizontal gene transfer?
- Short explanation of papers and take-home message:
 - Inevitability of Genetic Parasites (Iranzo et al., 2016)
 - Critical mutation rate in a population with horizontal gene transfer (Aston et al., 2017)
 - Indirect Fitness Benefits Enable the Spread of Host Genes Promoting Costly Transfer of Beneficial Plasmids (Dimitriu, et al., 2016)
 - Gene Transfer Agent Promotes Evolvability within the Fittest Subpopulation of a Bacterial Pathogen (Québatte *et al.*, 2017)
- Common ground & differences
- Conclusion
- References

Horizontal gene transfer (HGT)

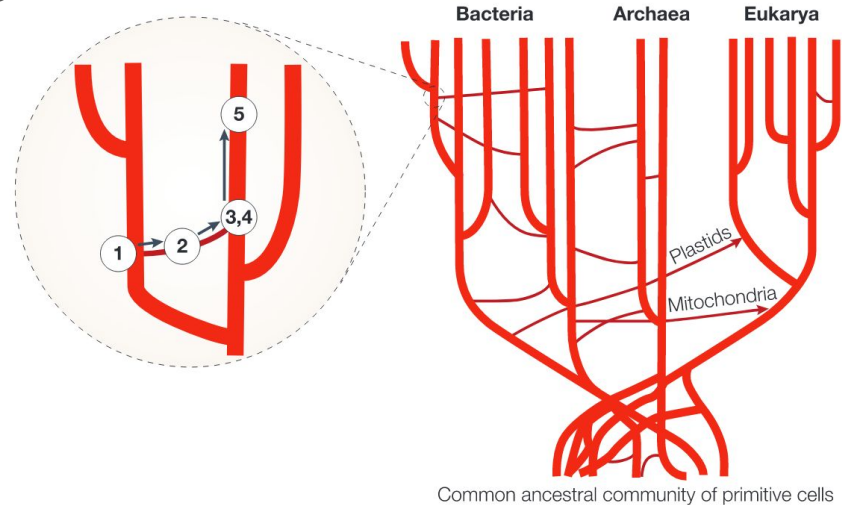
The transmission of genetic material other than from a parent to its offspring.

Plasmids, transposons or integrons can serve as vectors.

- ~31% of the bacterial genome has been acquired by HGT (Koonin 2001)
- Different ways: Transformation, Conjugation, Transduction via viruses

HORIZONTAL GENE TRANSFER: PERSPECTIVES AT A CROSSROADS OF SCIENTIFIC DISCIPLINES

Barth F. Smets and Tamar Barkay†*

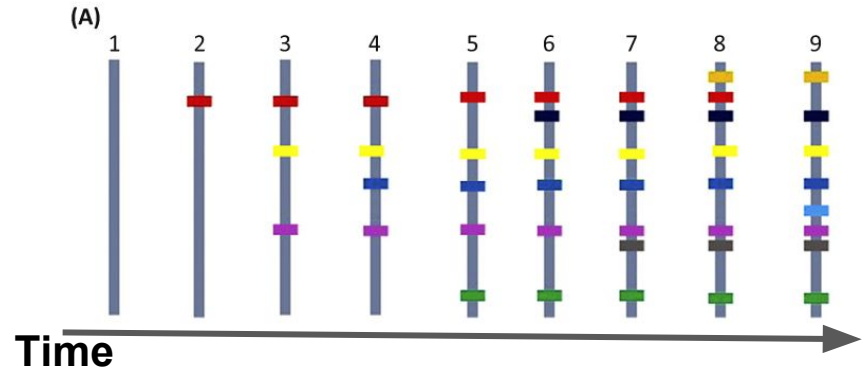


Muller's Ratchet

In the absence of recombination, finite populations are subject to irreversible deterioration through accumulation of deleterious mutations.

Some solutions:

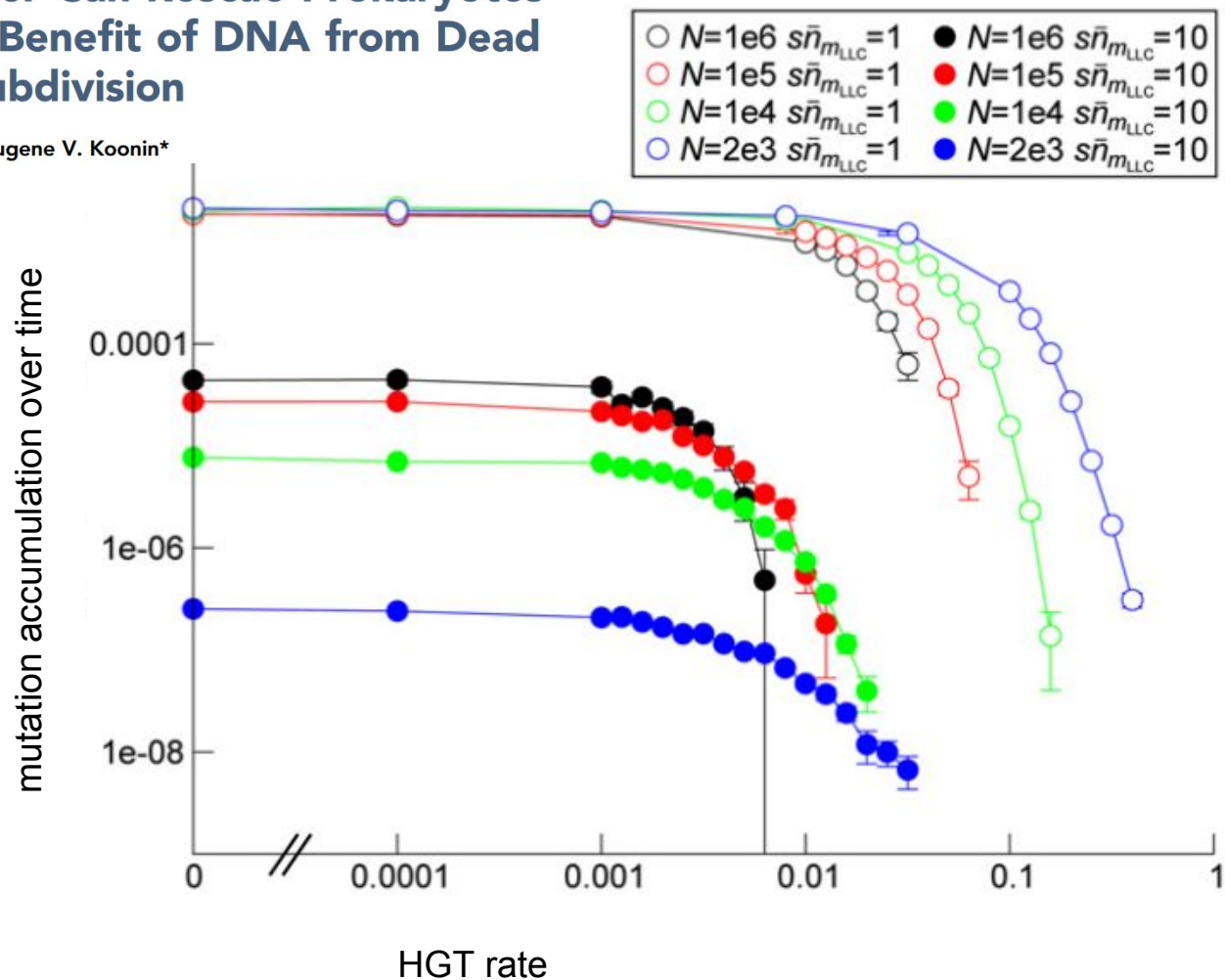
- Sexual reproduction
- Horizontal Gene Transfer
-



-> the U shape: with exceptions 'the main contribution to Muller's Ratchet are slightly deleterious mutations.'

Horizontal Gene Transfer Can Rescue Prokaryotes from Muller's Ratchet: Benefit of DNA from Dead Cells and Population Subdivision

Nobuto Takeuchi,^{*,†,1} Kunihiko Kaneko,[†] and Eugene V. Koonin^{*}



Inevitability of Genetic Parasites

Jaime Iranzo¹, Pere Puigbò^{1,2}, Alexander E. Lobkovsky¹, Yuri I. Wolf¹, and Eugene V. Koonin^{*,1}

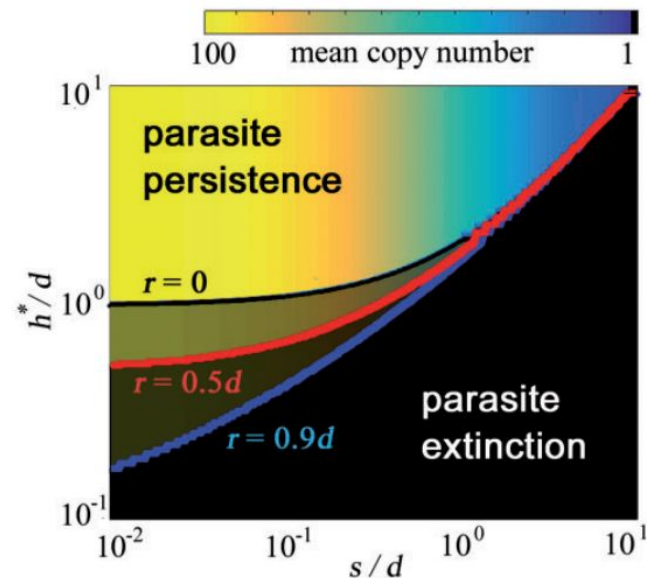
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- Clonal population (N),
- Genome of blocks
- Deleterious mutations
- Uptake of env. DNA (eDNA)
- HGT replacement of blocks
- + dynamics of parasitic copy numbers in host
- Parasite copy number: Proliferation, loss, HGT, purifying selection (fitness cost)
- Probability of infection via HGT \sim av. copy no. in pop.



h : HGT rate

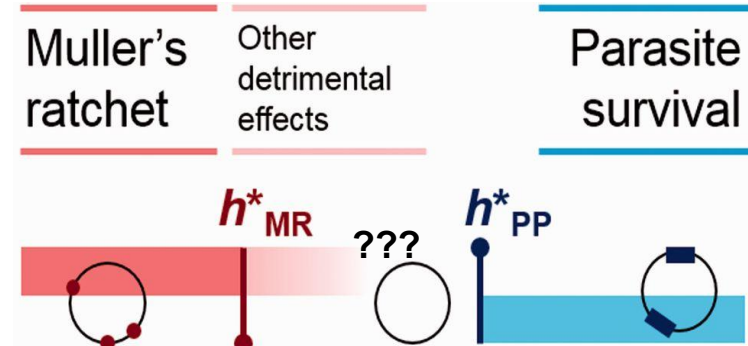
d : Loss (via deletions)

s : Cost of fitness to the host

r : Rate of proliferation

HGT makes genetic parasites inevitable

(Iranzo *et al.*, 2016)



Effective loss bias: d_e such that $h \geq d_e$

Effective size experiencing del. mut.: N_e

Simplified: A parasite persists, when

$$N_e * d_e < e \quad (2.7)$$

HGT makes genetic parasites inevitable

Prokaryotic genomes database (ATGC) for inferred loss and transfer rates for the mobilome.

$H_{MR}/\text{Loss ratio} \gg 1$ for both MGE and other genes

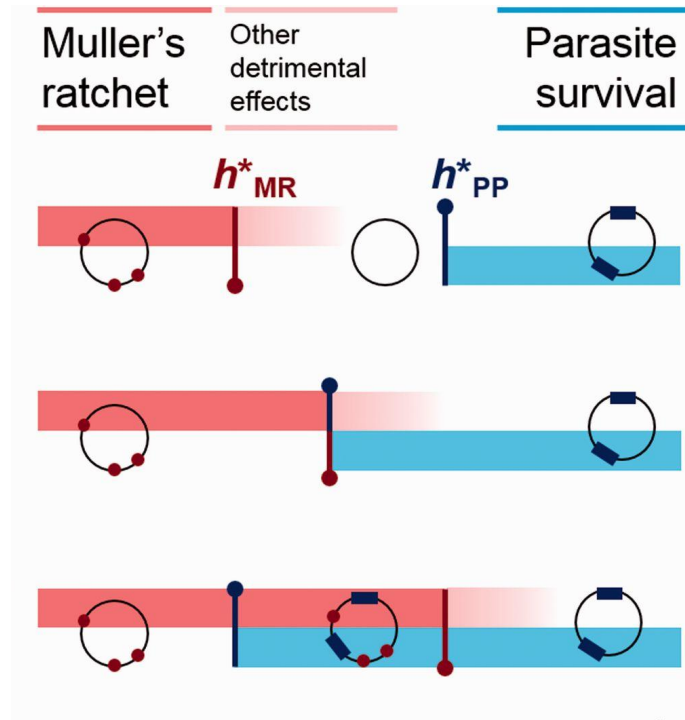
Considered average within-species nt variation:

$$N_e * d_e < 2.7 \text{ BUT conservative } > 2.7$$

Conclusion: Living on the edge

HGT makes genetic parasites inevitable,
but also ensures survival of non-mobilome genes
and rescue from Muller's ratchet.

(Iranzo *et al.*, 2016)



Critical mutation rate in a population with horizontal gene transfer (Aston *et al.*, 2017)

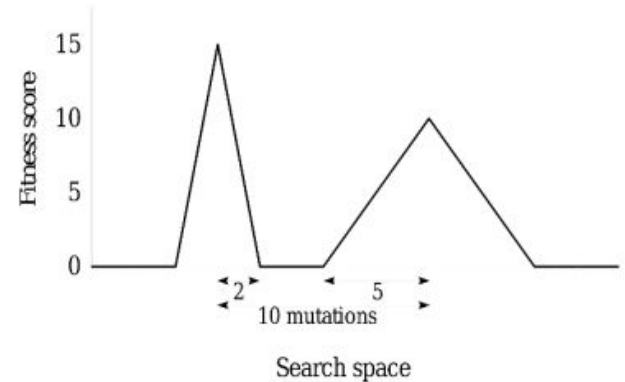
Sequence based model

Fitness: Hamming distance to closest peak.

Reproduction: cross-over & clonal

Tournament selection with 3 random individuals

Child undergoes HGT and point mutation



CMR: “the mutation rate at which 95% of 2000 runs lost peak 0 within 10,000 generations” -- exponential relationship with population size (eukaryotes)
(Error threshold)

Survival of the flattest (Wilke *et al.*, 2005)

HGT lowers the CMR, unless ...

(Aston *et al.*, 2017)

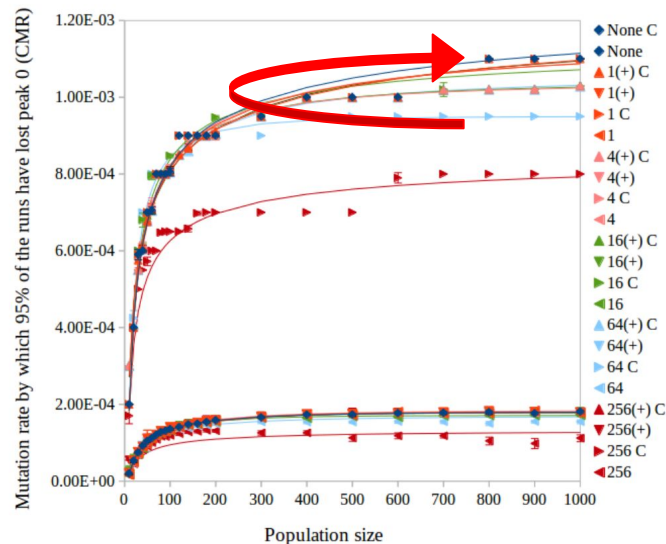
- 1) HGT reduces CMR in population with cross-over
- 2) ... especially larger segments
- 3) Higher CMR in clonal population
- 4) **HGT from only >0 fitness donors prevents decrease in CMR in clonal**

Exponential relationship: CMR and population size

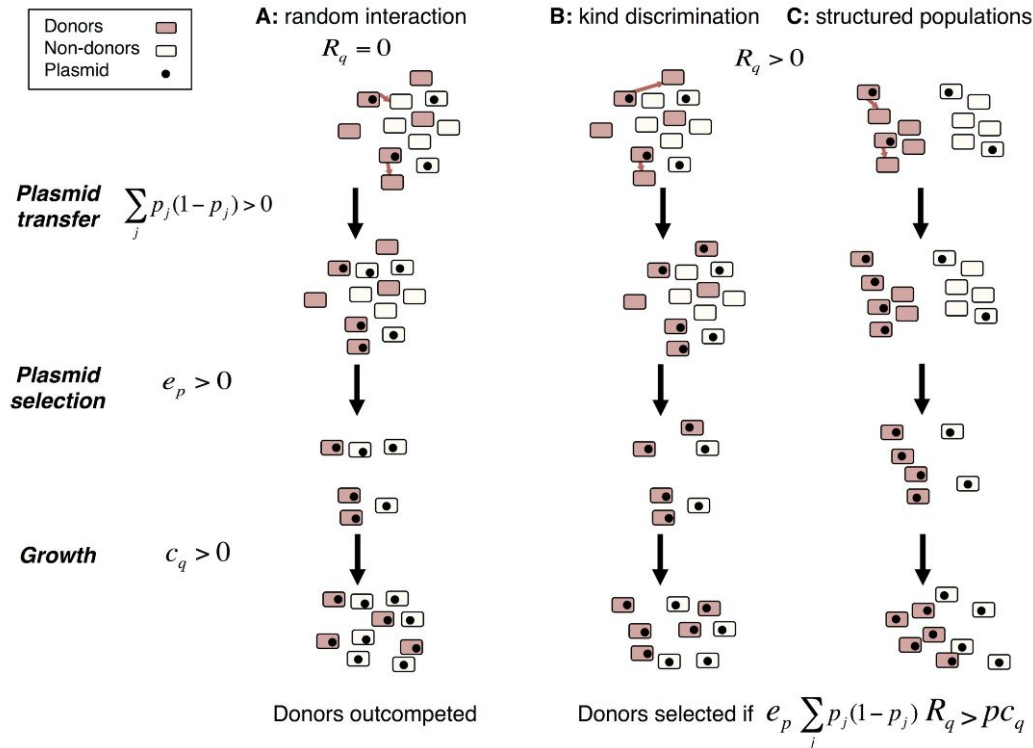
Implications for small populations?

→ lose the gained fit phenotype

Sequence model does not allow for neutrality



Indirect Fitness Benefits Enable the Spread of Host Genes Promoting Costly Transfer of Beneficial Plasmids (Dimitriu, *et al.*, 2016)



Selection of donors:

$$e_p \times \sum_j p_j(1-p_j) \times R_q > pc_q$$

plasmid benefits transfer efficiency relatedness among donors transfer cost

p plasmid frequency
 e_p plasmid benefits
 R_q relatedness among donors
 c_q transfer cost

$$b * R > c$$

Relatedness is determined by sharing an allele at the donor ability locus

(recipient is also a donor)

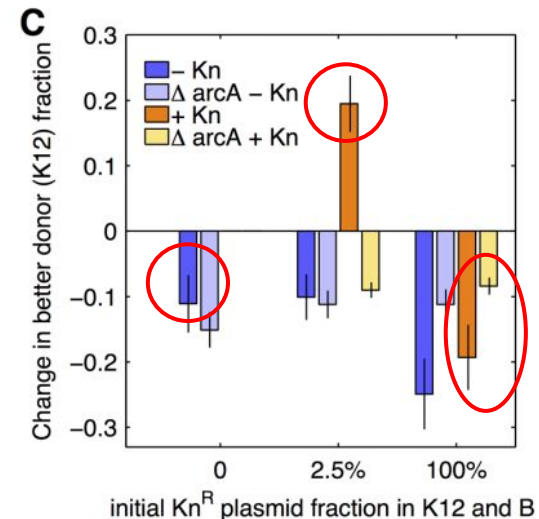
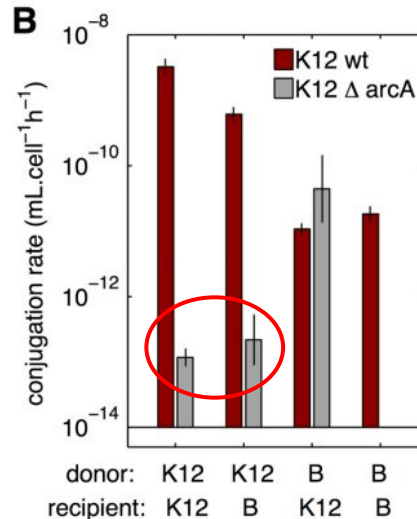
Donating a beneficial plasmid as altruistic behavior (Dimitriu, *et al.*, 2016)

Experimental: E. Coli strains K12 and B, different restriction enzymes.

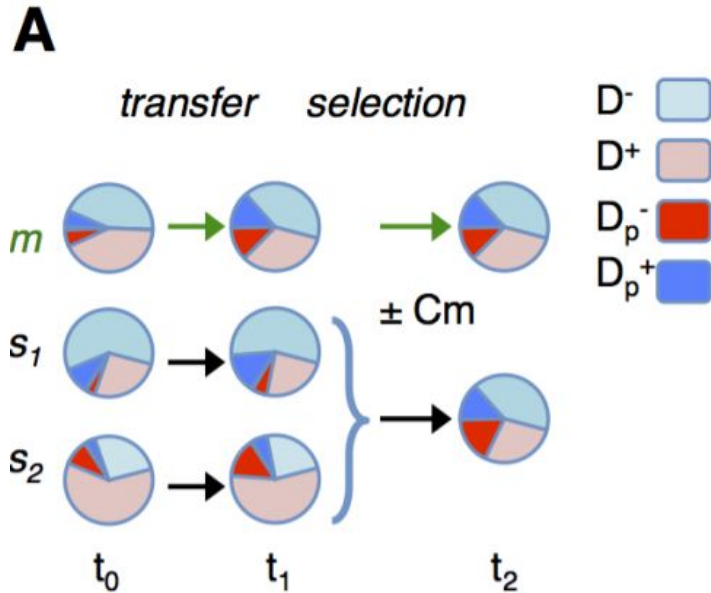
B) K12 'better donor'
arcA deletion reduces donor ability

C) K12 is selected when given
opportunity for plasmid transfer
&
donor ability is costly / altruistic

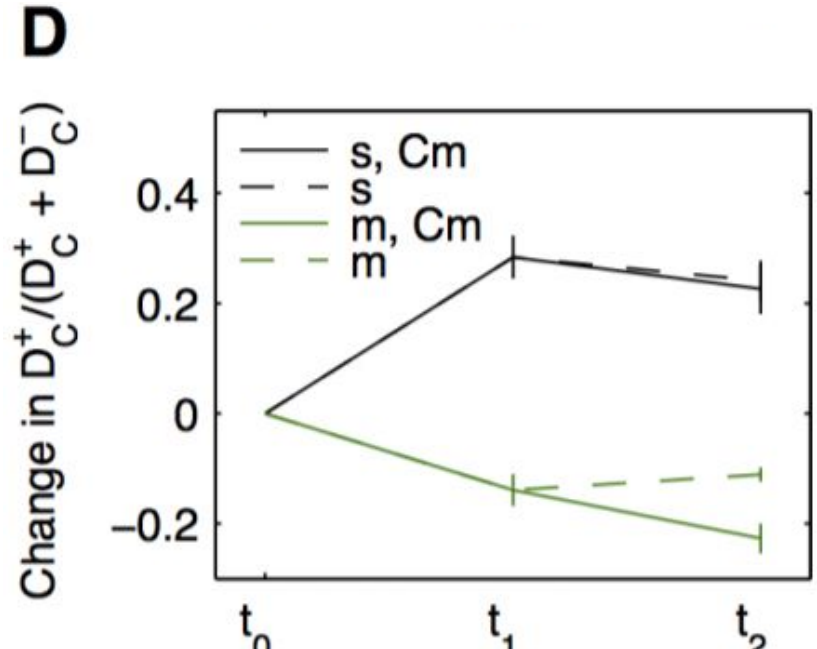
(arcA deletion diminishes difference)



“Structured” populations / high relatedness and selection of donor ability (Dimitriu, *et al.*, 2016)



s_1	90% D^-	10% D^+
s_2	10% D^-	90% D^+



Association between donor and discrimination alleles (Dimitriu, *et al.*, 2016)

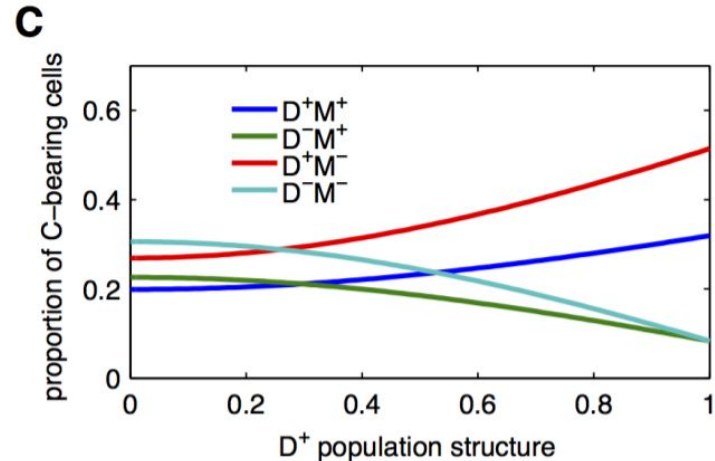
Simulation: can relatedness / population structure also emerge?

“Structure” is again unequal fraction in subpopulations.

M- mutant, discrimination allele: its plasmids will be degraded in wt cells

With increasing population structure
most plasmids end up in D+M-

**Linkage between discrimination and
donor alleles emerges.**



Indirect Fitness Benefits Enable the Spread of Host Genes Promoting Costly Transfer of Beneficial Plasmids (Dimitriu, *et al.*, 2016)

Main point:

Donor ability for beneficial plasmids can be selected for in a 1) 'structured population' or 2) with discrimination mechanism.

Critical points:

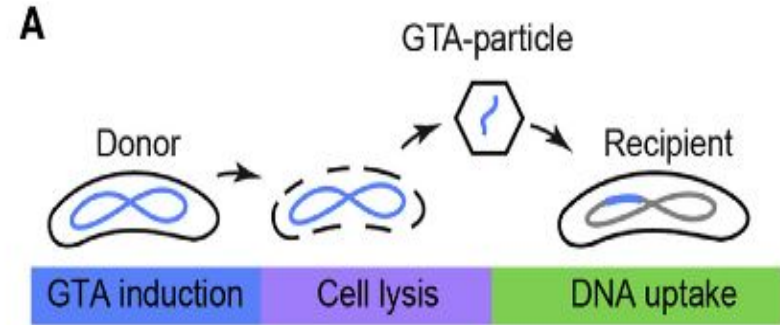
- Demonstration model - overfitted?
- No mutation? Binary phenotypes
- Enforced 'structure'
- Little degrees of freedom
- No neutrality

Experimental proof of concept, HGT mechanism in alpha proteobacteria *Bartonella* (Maxime Québatte 2017)

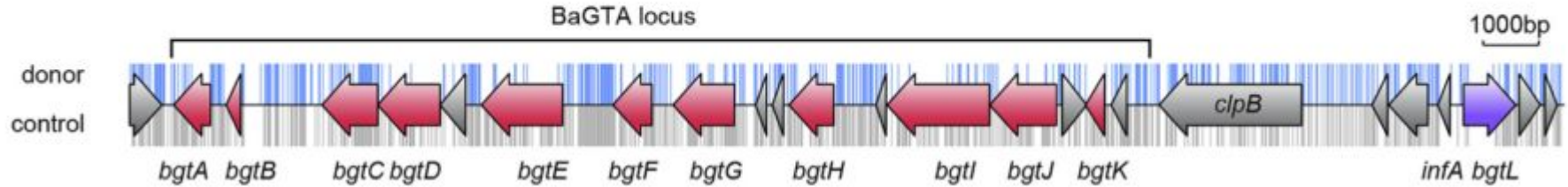
Gene transfer agents (GTA's):

Promotes HGT between cells through lysis and release of bacteriophage-like intermediates

- *Bartonella*-specific GTA (BaGTA)
 - Increase likelihood of genetic exchange
 - facilitates rapid adaptation to host-specific defence during infection
 - may help avoid Muller's Ratchet



Bartonella henselae GTA gene cluster



The GTA gene cluster contains phage:

- integrase
- capsid components
- tail fiber proteins
- base-plate
- endolysins

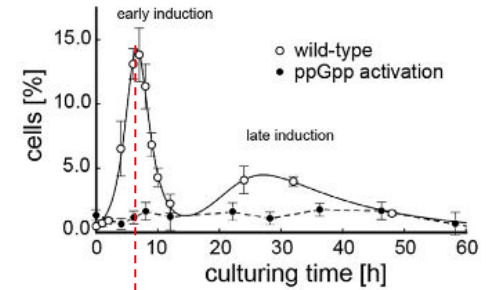
Very much a phage, though implicated to be strictly vertically transferred
“domesticated-phage”

BaGTA induction

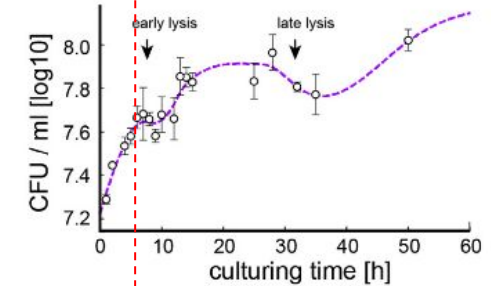
Distinct subpopulation of cells with induced BaGTA locus during rapid proliferation stage of cell culture, Followed by lysis and DNA uptake

Strangely there is a second peak of induction that gives no extra DNA uptake

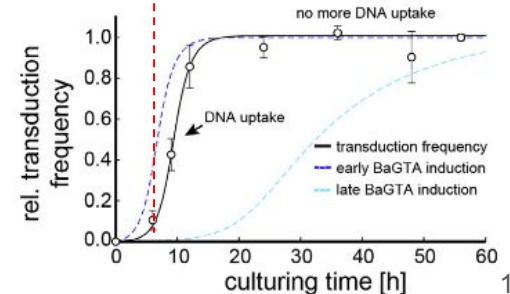
B BaGTA induction



C Cell lysis



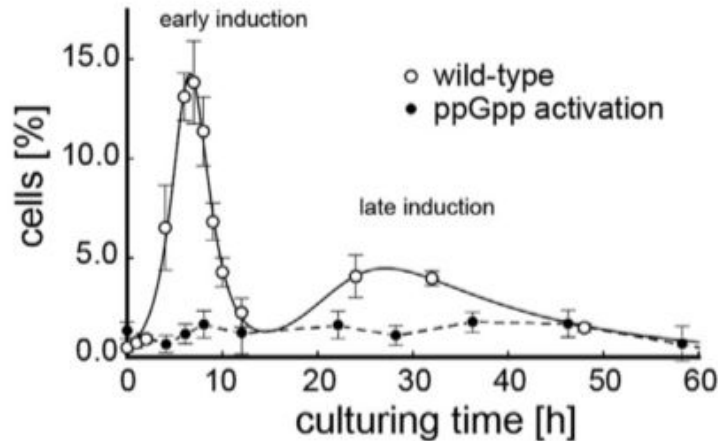
D DNA uptake



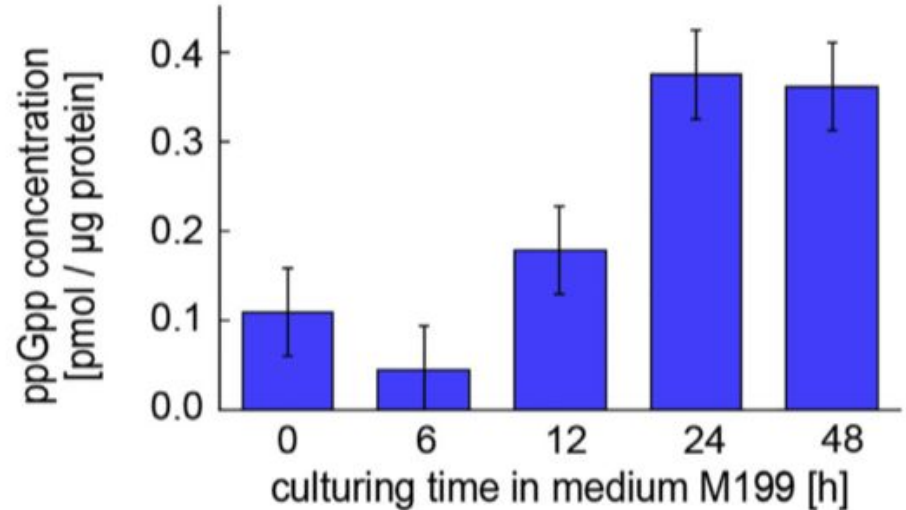
ppGpp alarmone cause strong repression of BaGTA

ppGpp: Leading to the bacterial cell shutting down growth, entering dormant survival mode

B BaGTA induction



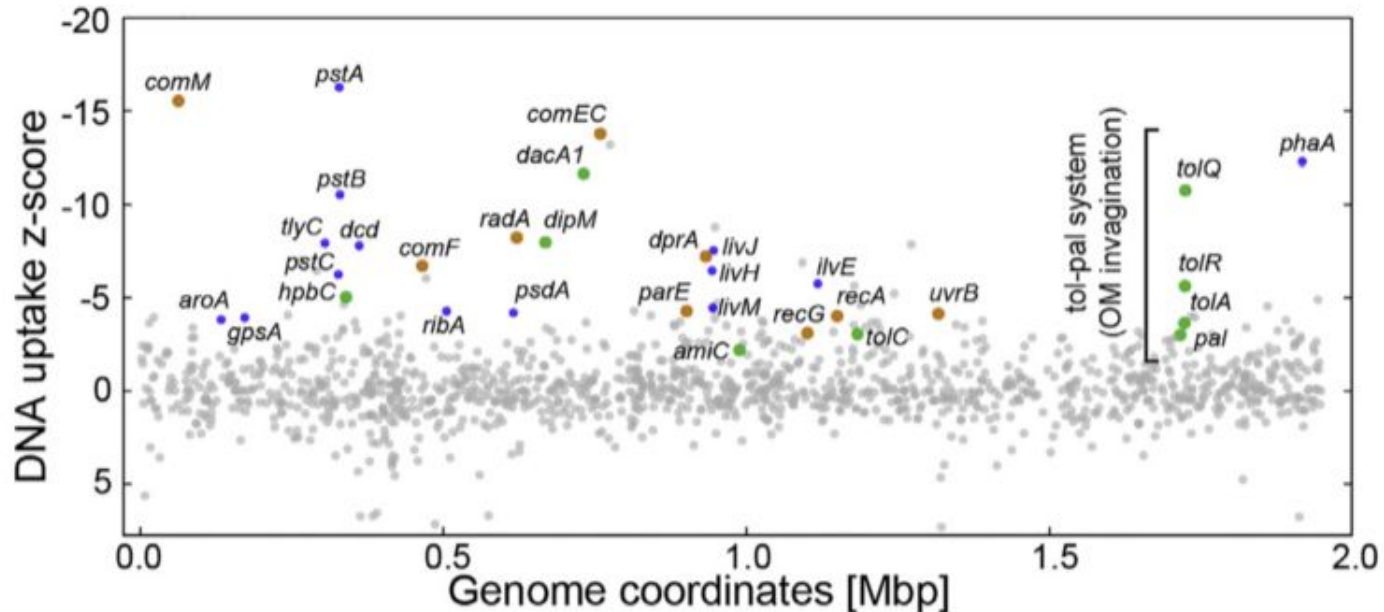
B



Genes involved in the uptake and incorporation of BaGTA

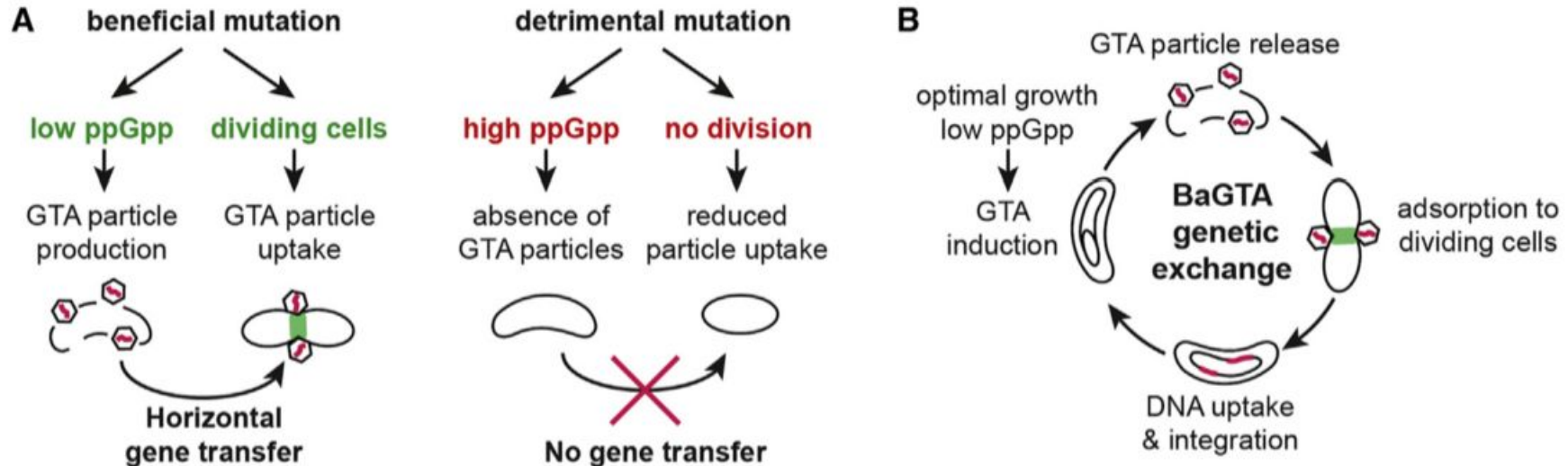
A

Genome-wide identification of BaGTA susceptibility genes



BaGTA Promotes Genetic Exchange among the Fittest Subpopulation of cells

Fittest defined as replicating cells



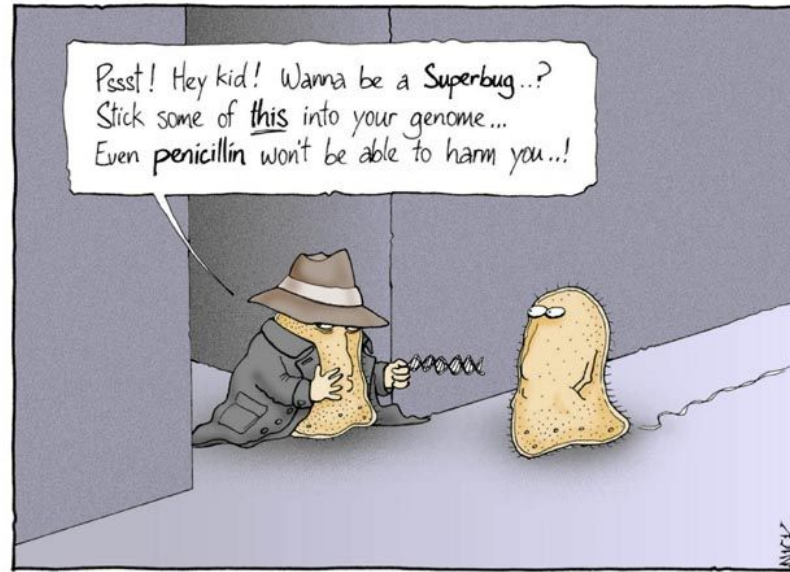
Discussion

- HGT important for evolution because escaping Muller's Ratchet, having implications for evolvability
- HOWEVER:
 - HGT can be exploited by parasites
 - Lowers the Critical mutation rate, causing the survival of the flattest
 - HGT can be seen as altruistic burden, where a discrimination mechanisms are needed
- HOWEVER:
 - HGT from the fittest in a population might circumvent the altruistic burden and lowering CMR
 - Parasites are not per definition detrimental

There are all these multilevel effects that are still being overseen

Questions

HGT: evolution. regulation and consequences



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.