

Viruses as an intrinsic feature of life and a key factor of evolution

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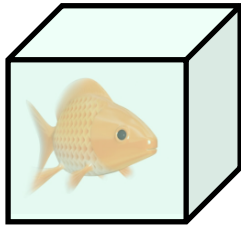
Salzburg, July 5, 2018

NCBI: Evolutionary Genomics Group



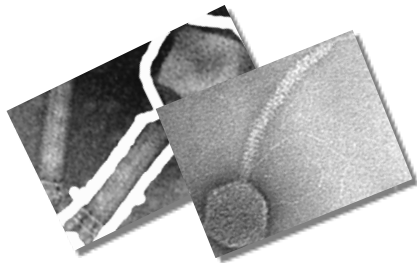
<http://www.ncbi.nlm.nih.gov/research/groups/koonin/>

Viruses are the dominant entities in the biosphere – physically and genetically – as shown by viral metagenomics – virome studies



1 cm³ of seawater contains 10⁶-10⁹ virus particles

Suttle, C.A. (2005) *Nature* 437:356



There are millions of diverse bacteriophage species in the water, soil, and gut

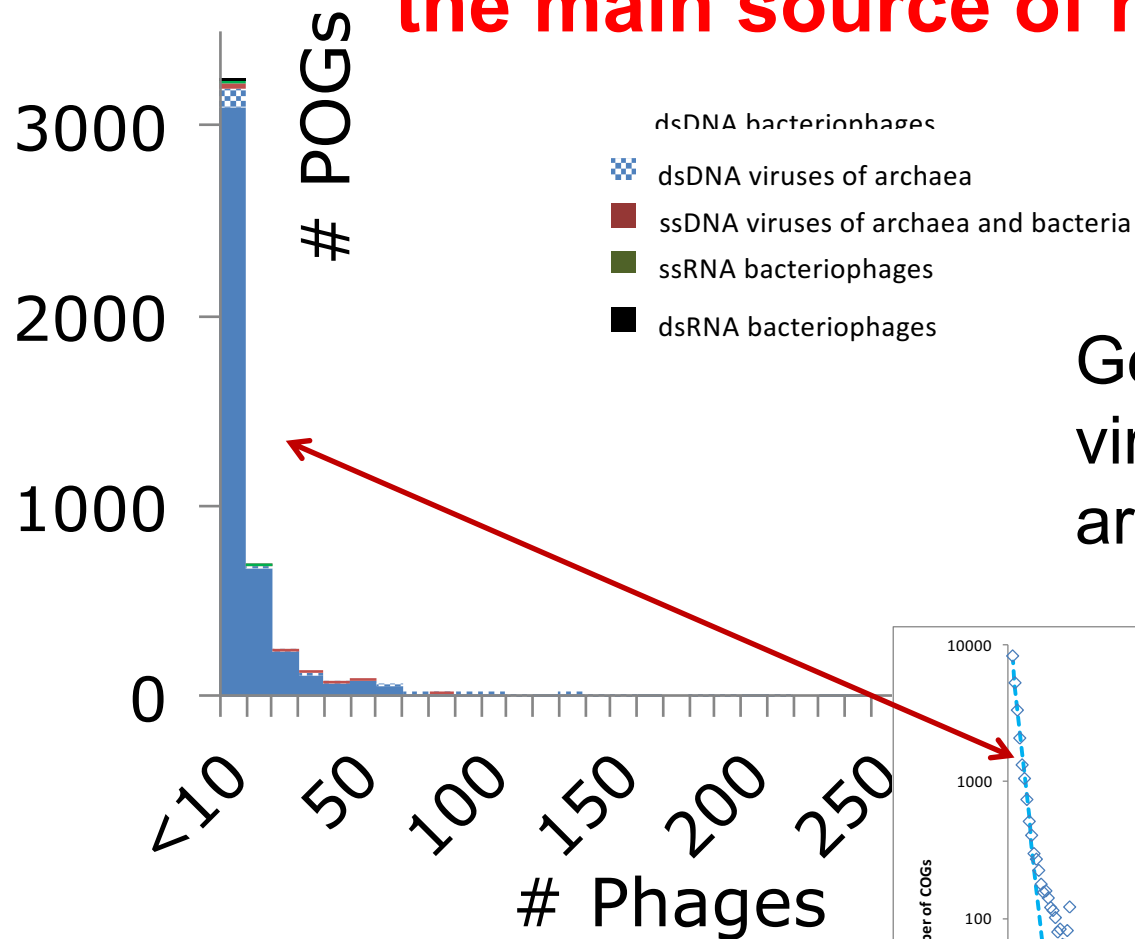
Edwards and Rohwer (2005) *Nat. Rev. Microbiol.* 3:504

• *Viruses are the most abundant biological entities in the biosphere: 10-100 virus particles per cell in most habitats*

Human body: ~10¹⁴ human cells vs ~10¹⁵ bacteria vs ~10¹⁶ viruses

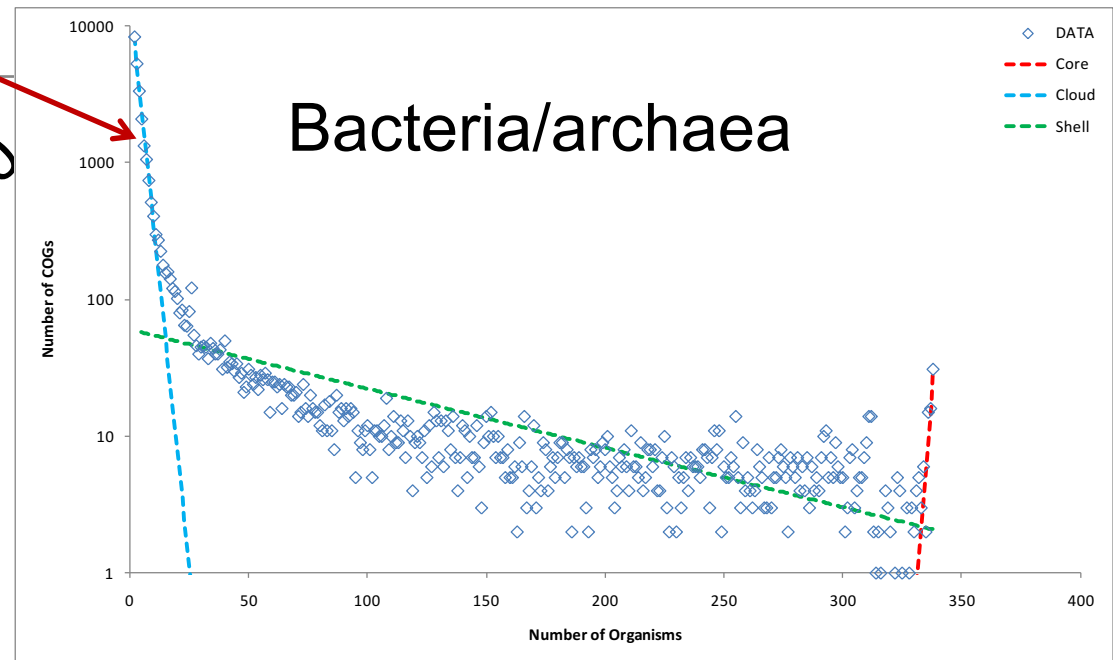
Earth-wide counts: ~5x10³⁰ bacteria vs ~10³² viruses

Viruses: “Infinite” pool of genetic diversity – the main source of new genes on earth?



Kristensen et al. J. Bacteriol 2013

Gene frequency plots for viruses and cellular life forms are drastically different



Koonin, Wolf 2008

Inevitability of parasites

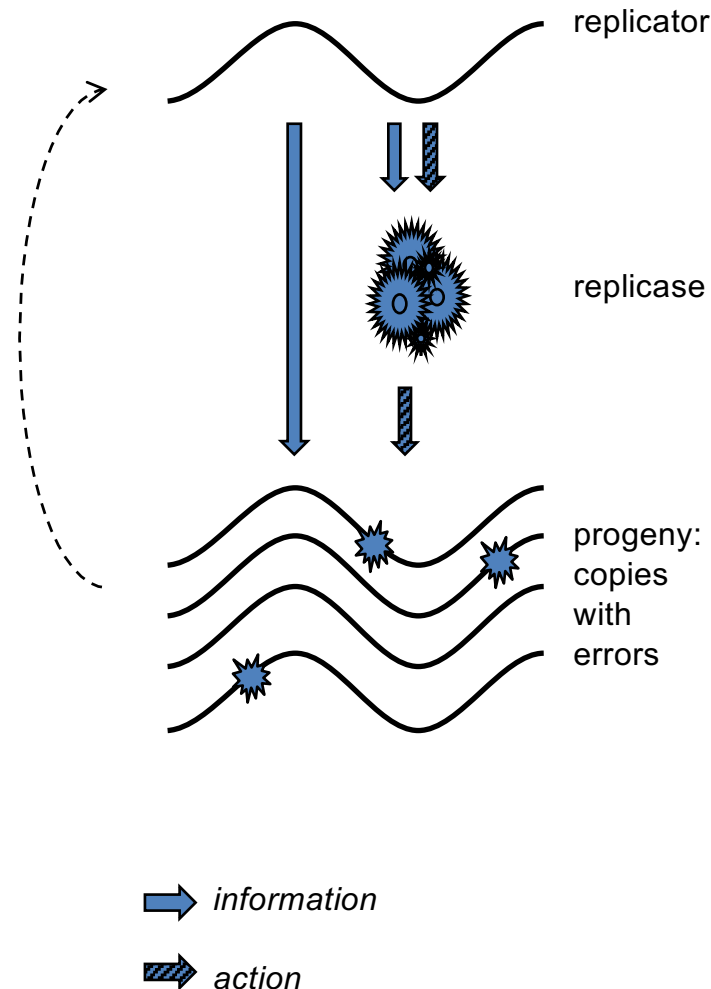
Parasites (cheaters) evolve in **ANY** replicator system (e.g. hypercycle): as soon as there is a resource to steal such as a replicase, someone will find a way to live by stealing it

More formally: **parasite-protected states of replicators are thermodynamically unstable**

Maynard Smith J (1979) Hypercycles and the origin of life. Nature 280:445–446

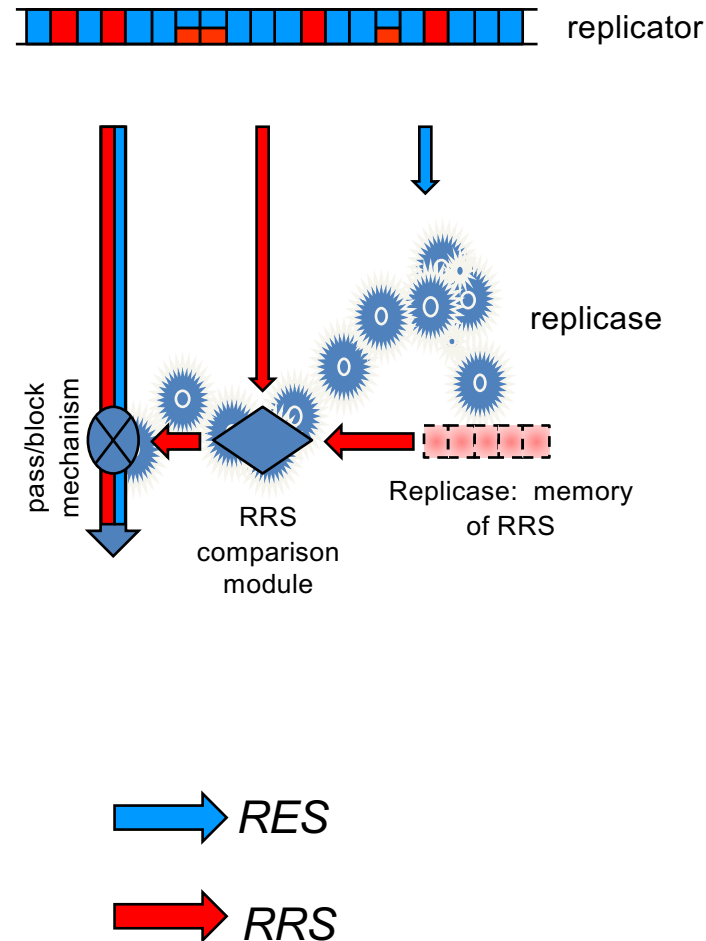
Koonin, Wolf, Katsnelson. Inevitability of the emergence and persistence of genetic parasites caused by evolutionary instability of parasite-free states. Biol Direct 2017
<http://www.biorxiv.org/content/early/2017/08/30/182410>

The simplest replicator systems



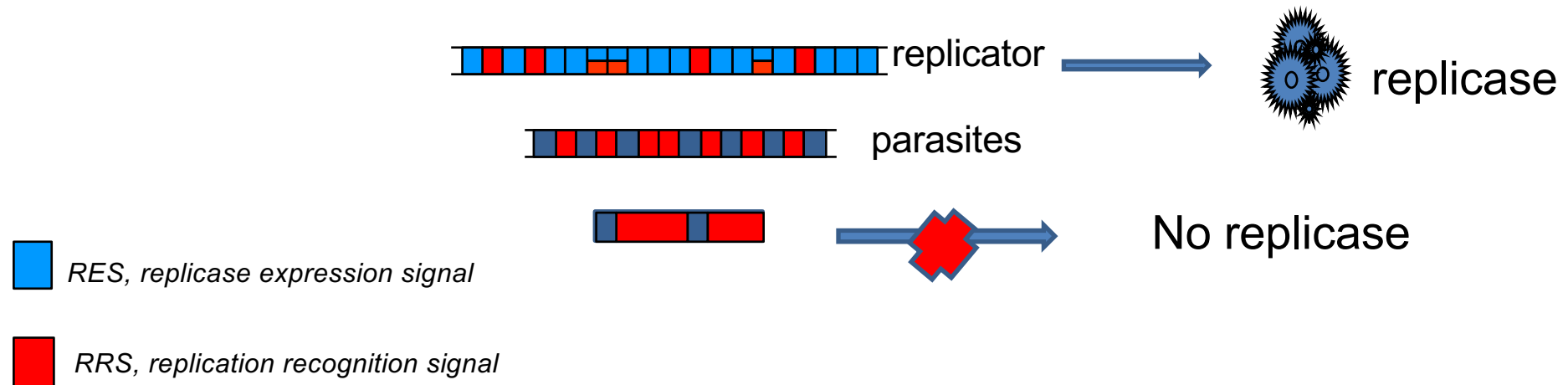
Koonin, Wolf, Katsnelson. Inevitability of the emergence and persistence of genetic parasites caused by evolutionary instability of parasite-free states. Biol Direct 2017
<http://www.biorxiv.org/content/early/2017/08/30/182410>

Replicase expression signal (RES) Replicase recognition signal (RRS)



Koonin, Wolf, Katsnelson. Inevitability of the emergence and persistence of genetic parasites caused by evolutionary instability of parasite-free states. Biol Direct 2017
<http://www.biorxiv.org/content/early/2017/08/30/182410>

Parasites retain replicase recognitions signal but lose replication expression signal



Unique, minimum entropy parasite-protected state: **RRS=RES**

vs

Numerous routes of parasite evolution

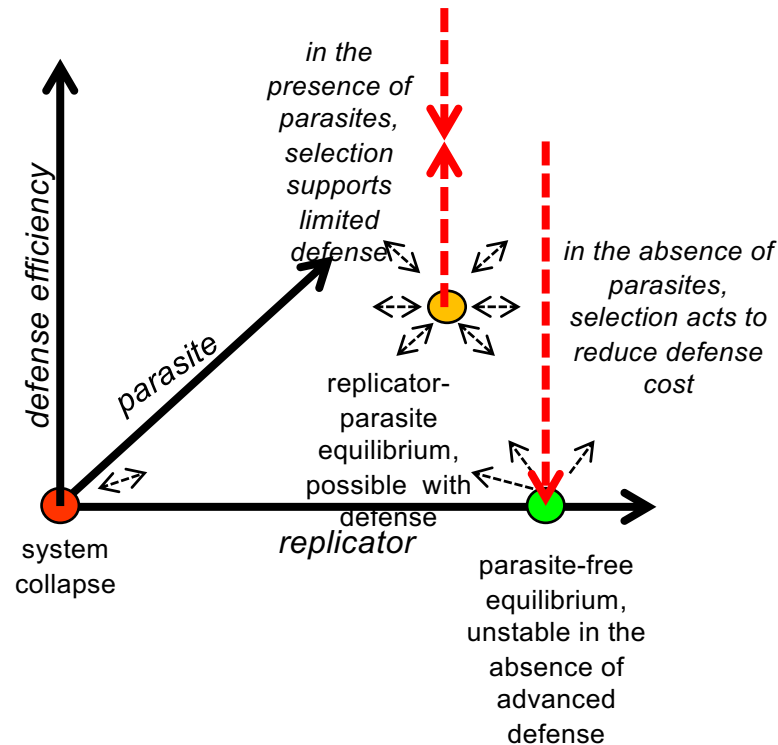


**Parasite-protected state is inherently (thermodynamically)
Unstable: cost of information, Landauer Principle**

Koonin, Wolf, Katsnelson. Inevitability of the emergence and persistence of genetic parasites caused by evolutionary instability of parasite-free states. Biol Direct 2017

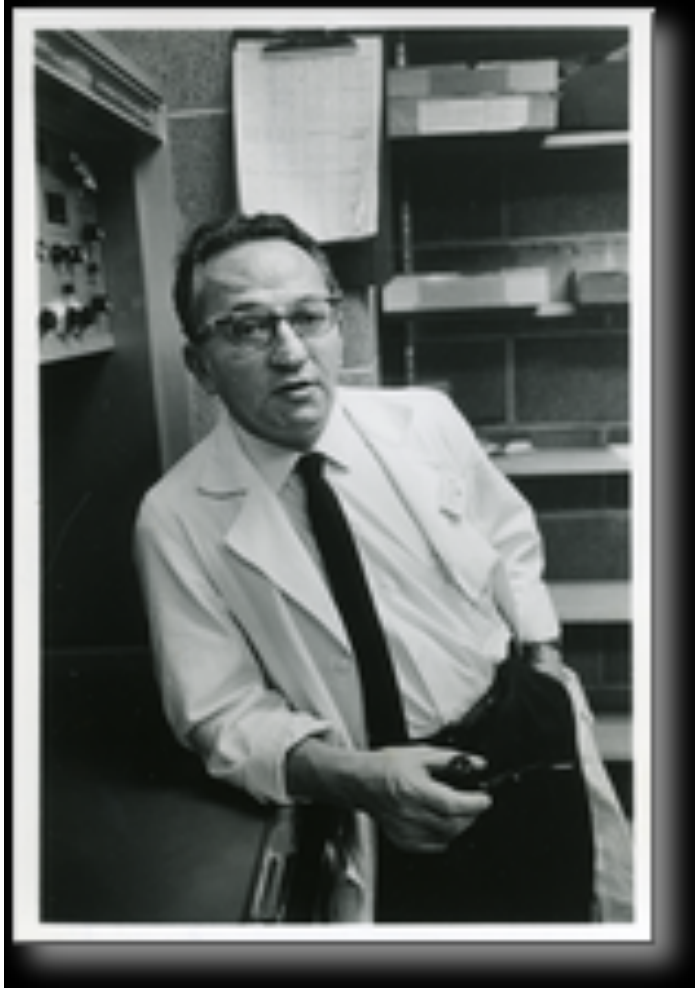
<http://www.biorxiv.org/content/early/2017/08/30/182410>

Only host-parasite equilibria are stable



Koonin, Wolf, Katsnelson. Inevitability of the emergence and persistence of genetic parasites caused by evolutionary instability of parasite-free states. Biol Direct 2017
<http://www.biorxiv.org/content/early/2017/08/30/182410>

Illustration in classical experiments: the **Spiegelman Monster**



Sol Spiegelman, 1914-1983

Mills DR, Peterson RL, Spiegelman S. An extracellular Darwinian experiment with a self-duplicating nucleic acid molecule. Proc Natl Acad Sci U S A. 1967 Jul;58(1):217-24

Kacian DL, Mills DR, Kramer FR, Spiegelman S. A replicating RNA molecule suitable for a detailed analysis of extracellular evolution and replication. Proc Natl Acad Sci U S A. 1972 Oct;69(10):3038-42

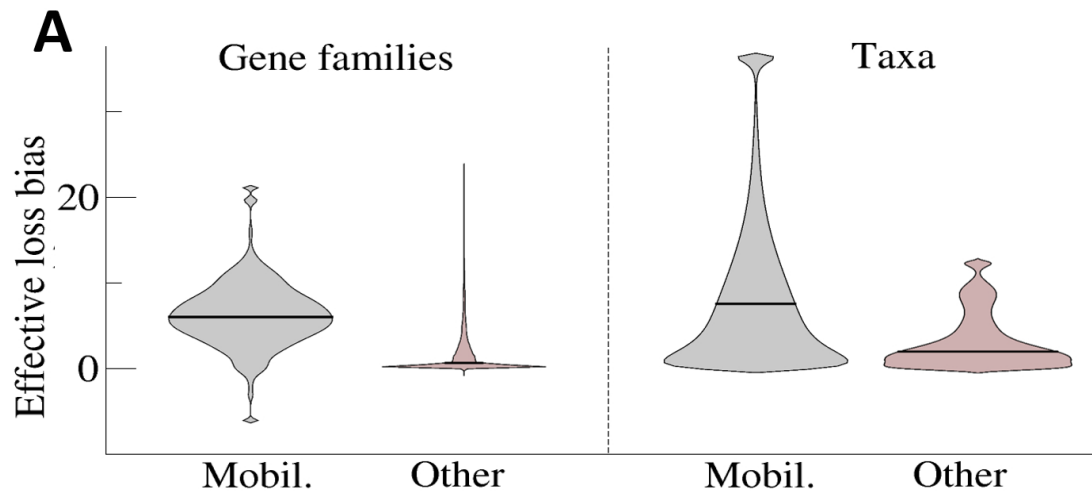
From 3500 nt (Q β) to 218 nt in 75 serial Passages

Complete loss of RES

Inevitability of genetic parasites/ selfish elements in the cellular world: is it possible to purge parasites?

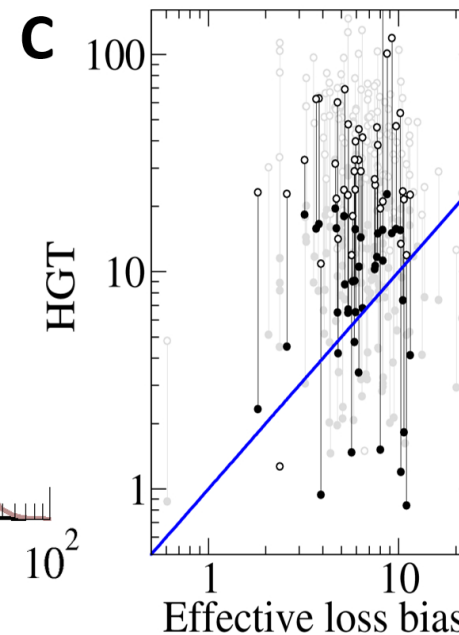
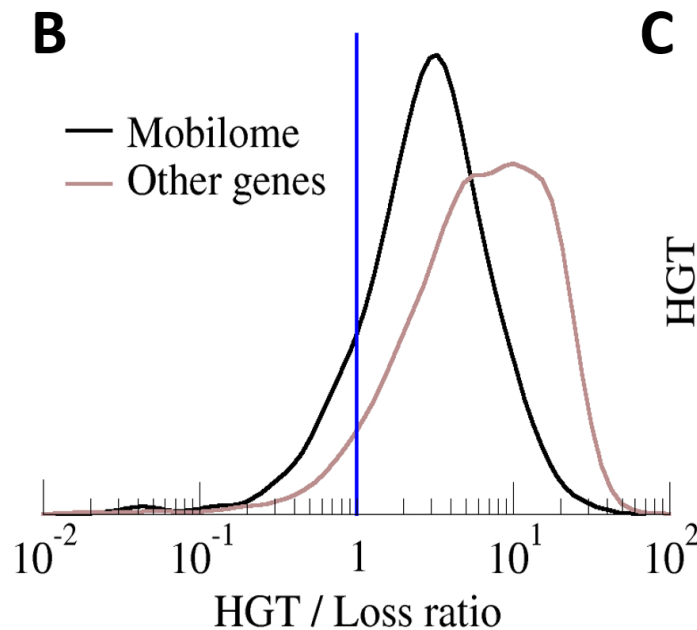
- (Almost) all cellular life forms are hosts to diverse genetic parasites with various levels of autonomy including plasmids, transposons and viruses
- Theoretical modeling of the evolution of primordial replicators indicates that parasites ('cheaters') necessarily evolve in such systems and can be kept at bay primarily via compartmentalization
- Given the (near) ubiquity, abundance and diversity of genetic parasites, the question becomes pertinent: **are such parasites intrinsic to life?**
- At least in prokaryotes, the persistence of parasites is linked to the rate of horizontal gene transfer (HGT)
- Asexual clonal populations are doomed to extinction by accumulation of deleterious mutations: **Muller's ratchet**
- $HGT > \text{threshold}$ - **escape from Muller's ratchet**
- $HGT > \text{threshold}$ - **parasite persistence**
- $h^*_{MR} > h^*_{PP}$ - **no chance to purge parasitic selfish elements**

Testing the parasite persistence condition on 35 clusters of closely related bacterial and archaeal genomes



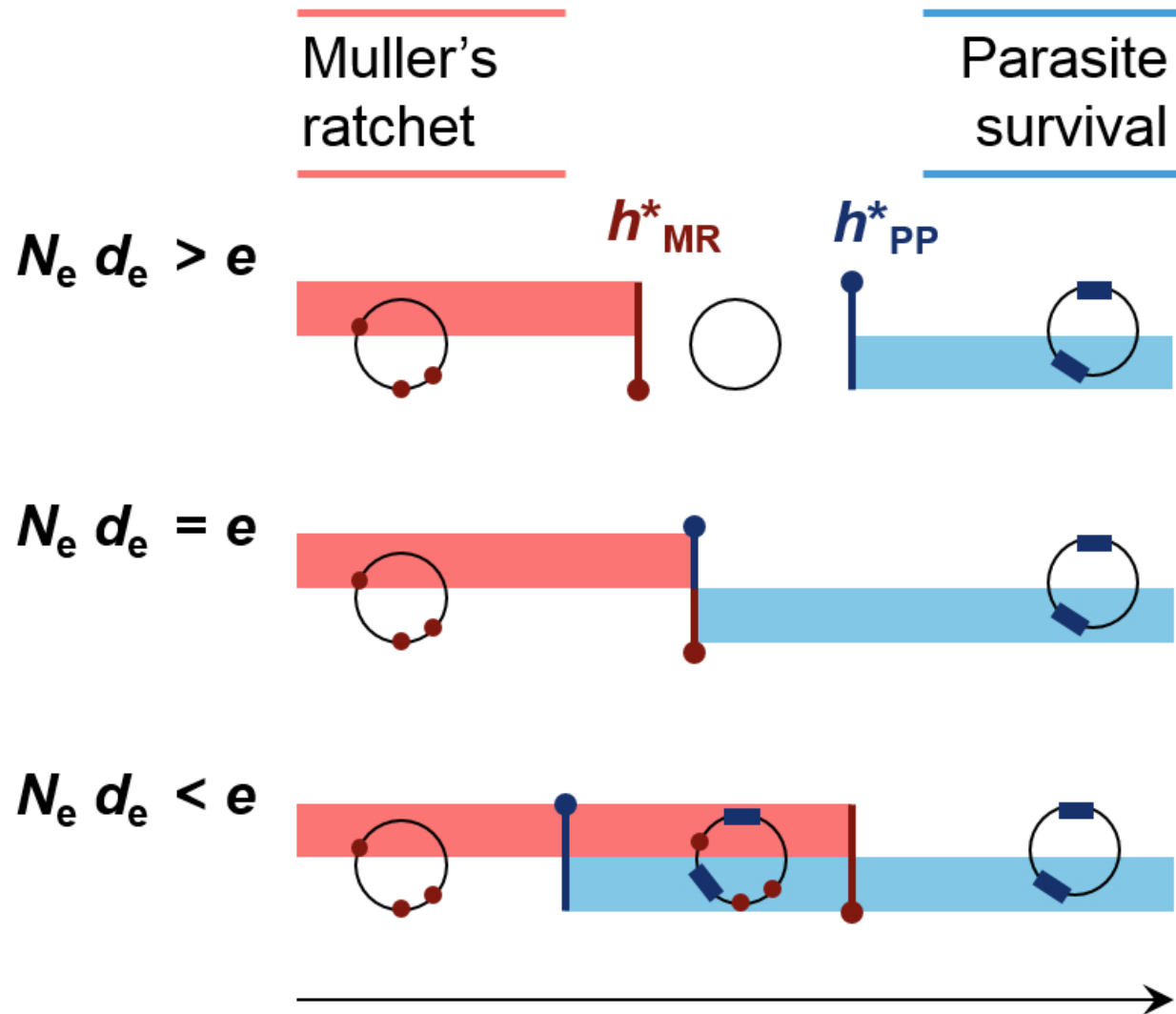
Persistence condition:

$$h > d_e$$



Holds for most microbes and most gene families

Between a rock and a hard place: Muller's ratchet vs parasite persistence – can microbes eliminate parasites by lowering HGT rate?



N_e , effective population size; d_e , effective deletion bias
HGT rate

**For most bacterial and archaeal genes,
even those devoid of active proliferation
capacity:**

$$h^*_{MR} > h^*_{PP}$$

**Thus, persistence of genetic parasites/selfish elements
is the **price to pay for maintenance of host genome
integrity** and hence inevitable;
moreover, most genes tend to be “selfish”**

- **Emergence and persistence of selfish genetic elements/viruses are inevitable in any evolving replicator system/population:**

A major biological universal

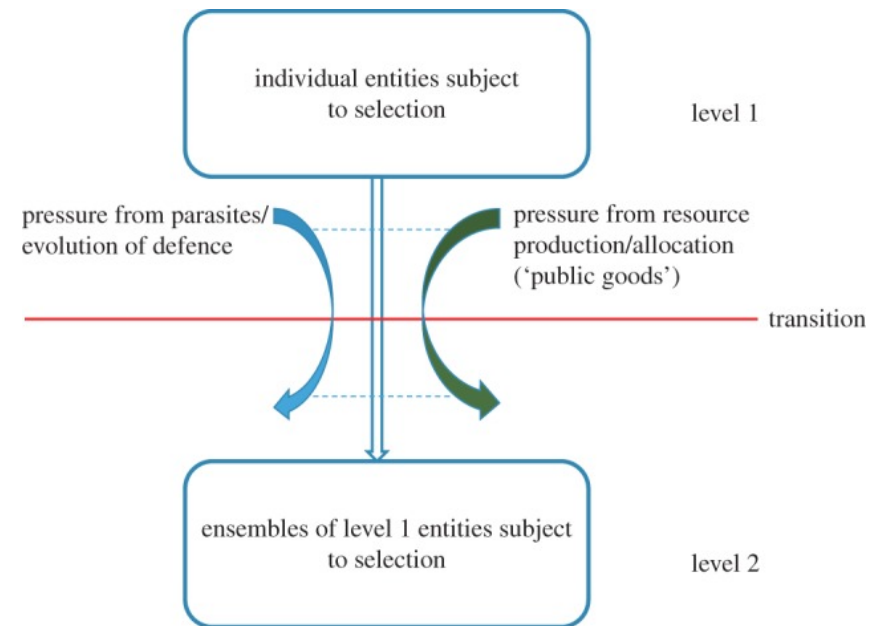
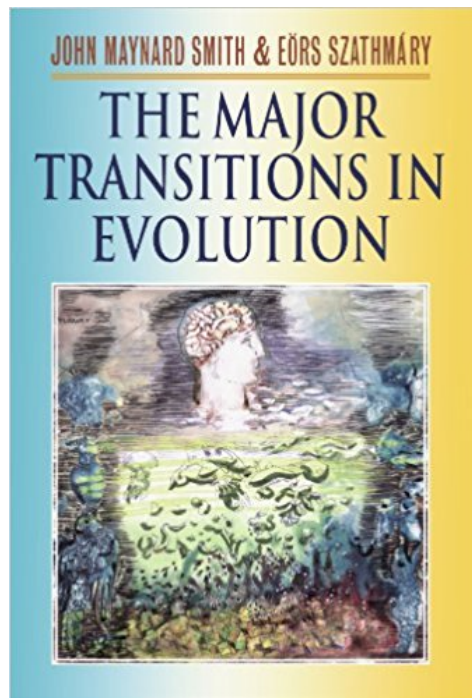
- **Perennial parasite-host arms race drove evolution of cellular organisms including the first cells, multicellularity and most likely other major evolutionary transitions**

Major transitions in evolution

Evolutionary Transition in Individuality:

New levels of selection

- Origin of cells
- Eukaryotic cells
- Multicellularity
- Eusociality
- Society



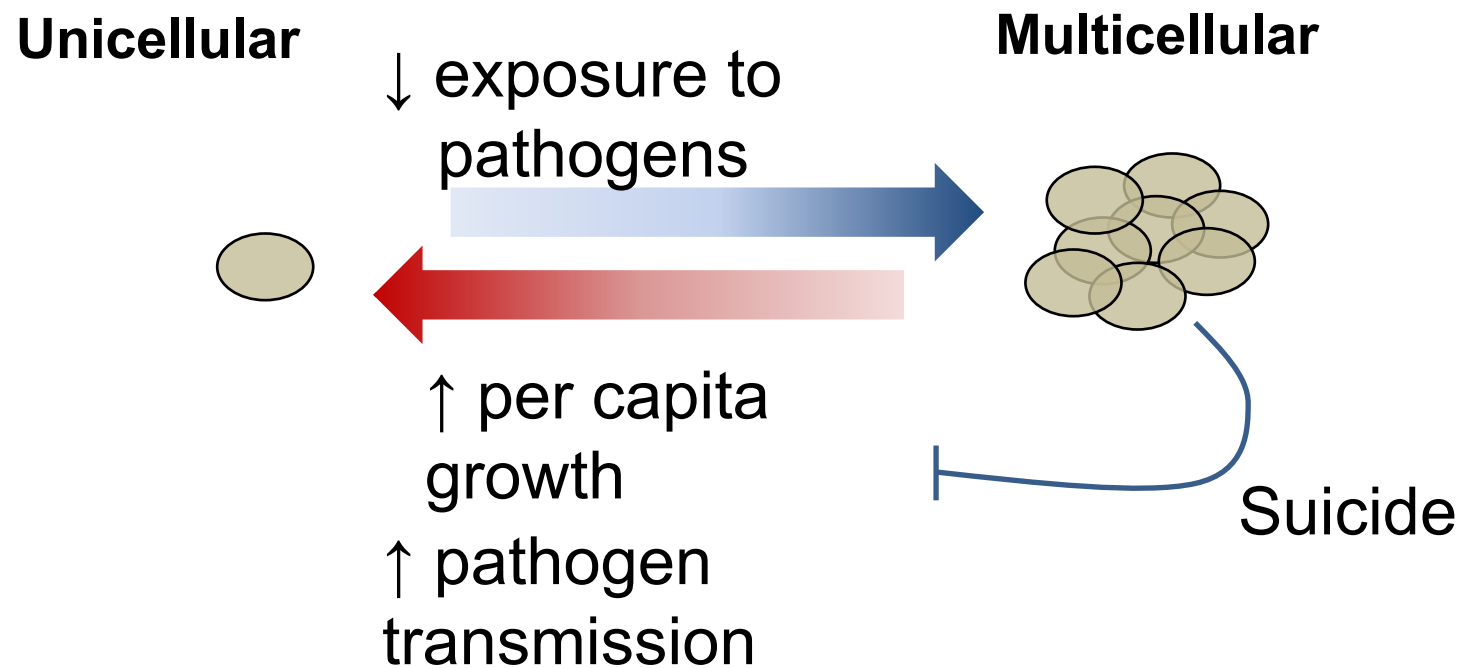
**Parasites promote evolution of complexity
and major evolutionary transitions:
Genetic parasites and evolution of
multicellularity**

Parasites drive evolution of complexity, in particular, compartmentalization

The class of replicators customarily called “parasites” is known to play important roles for the evolutionary dynamics of RNA-like replicator systems. Parasites are molecules that do not catalyze replication of other molecules but can be replicated by the catalysts, possibly at a faster rate than the catalysts themselves. **Under well-mixed conditions, the parasite can bring a replicator system to extinction by (over)exploiting catalysts.** Because of this inherent instability of RNA-like replicator systems against the parasite, it is necessary to consider spatial structure in the population of replicators and the discreteness of the population, which can prevent the extinction caused by parasites. Moreover, if extinction is prevented through spatial pattern formation, the parasite can contribute to the evolution of complexity in RNA-like replicator systems.

Takeuchi N, Hogeweg P. The role of complex formation and deleterious mutations for the stability of RNA-like replicator systems. J Mol Evol. 2007 Dec;65(6):668-86.

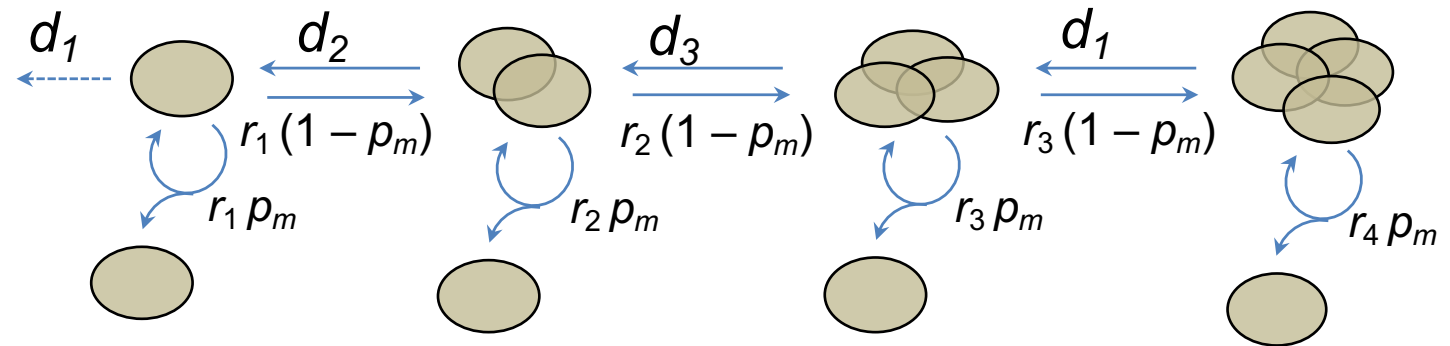
Selection pressures involved in pathogen-host interaction



Population model

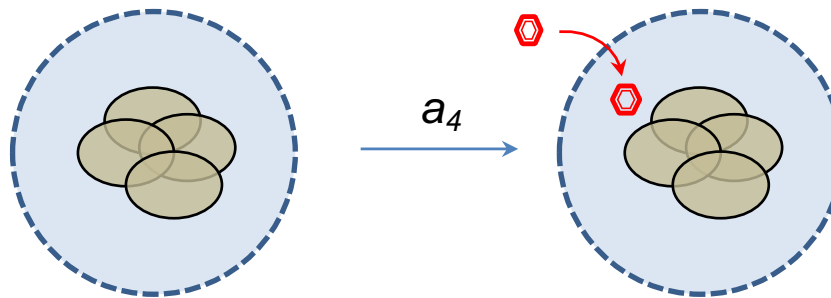
Replication / Death

$$\begin{aligned} d_k &= k d \\ r_k &= k^\gamma r \\ 2/3 \leq \gamma &\leq 1 \end{aligned}$$



Pathogen arrival

$$\begin{aligned} a_k &= k^\alpha a \\ \alpha &= 2/3 \end{aligned}$$

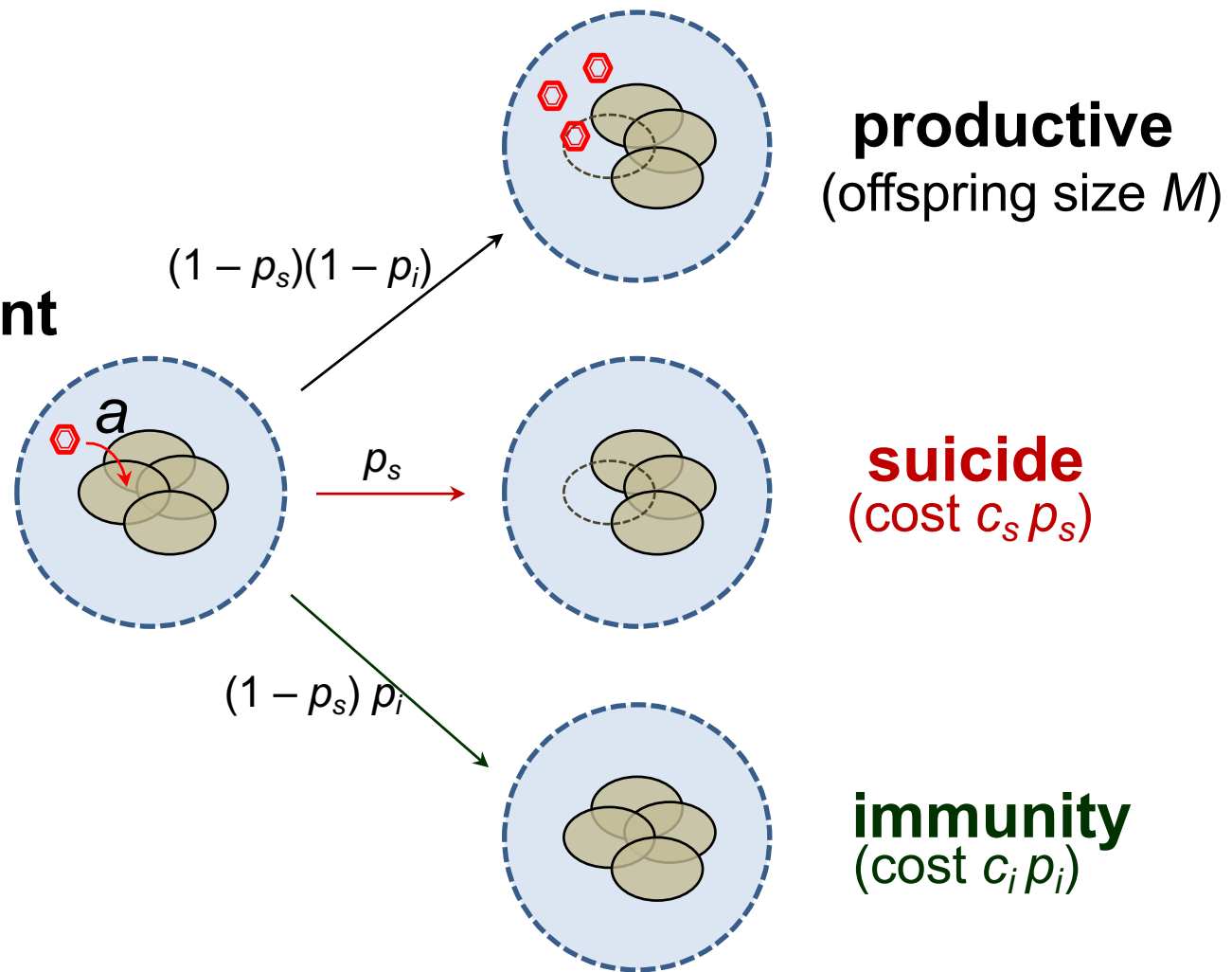


Tradeoff: Opposite effects of multicellularity on replication and pathogen exposure

- **Multicellularity protects against parasite through suicide**

Population model

Infection event



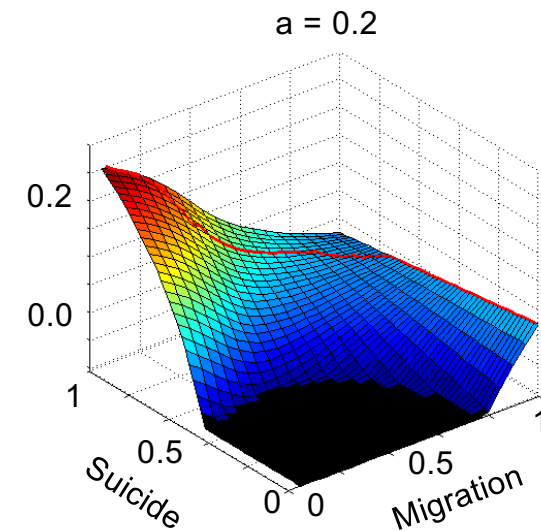
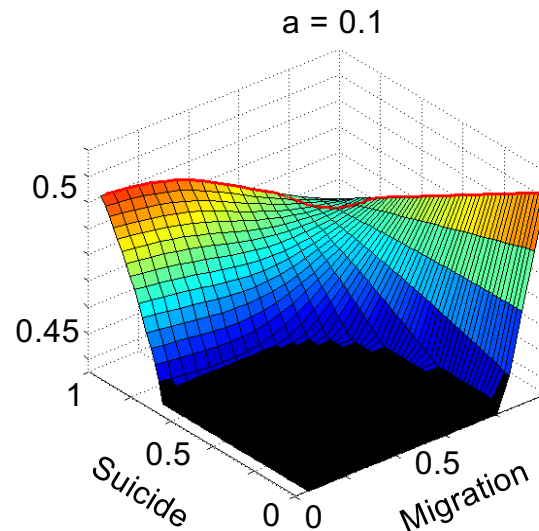
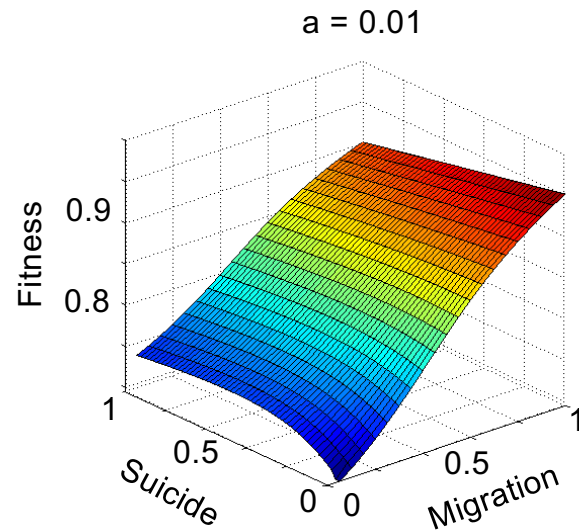
Evolution of multicellularity/programmed cell suicide under the pressure of pathogens

**Singletons,
no suicide**

increasing pathogen
pressure

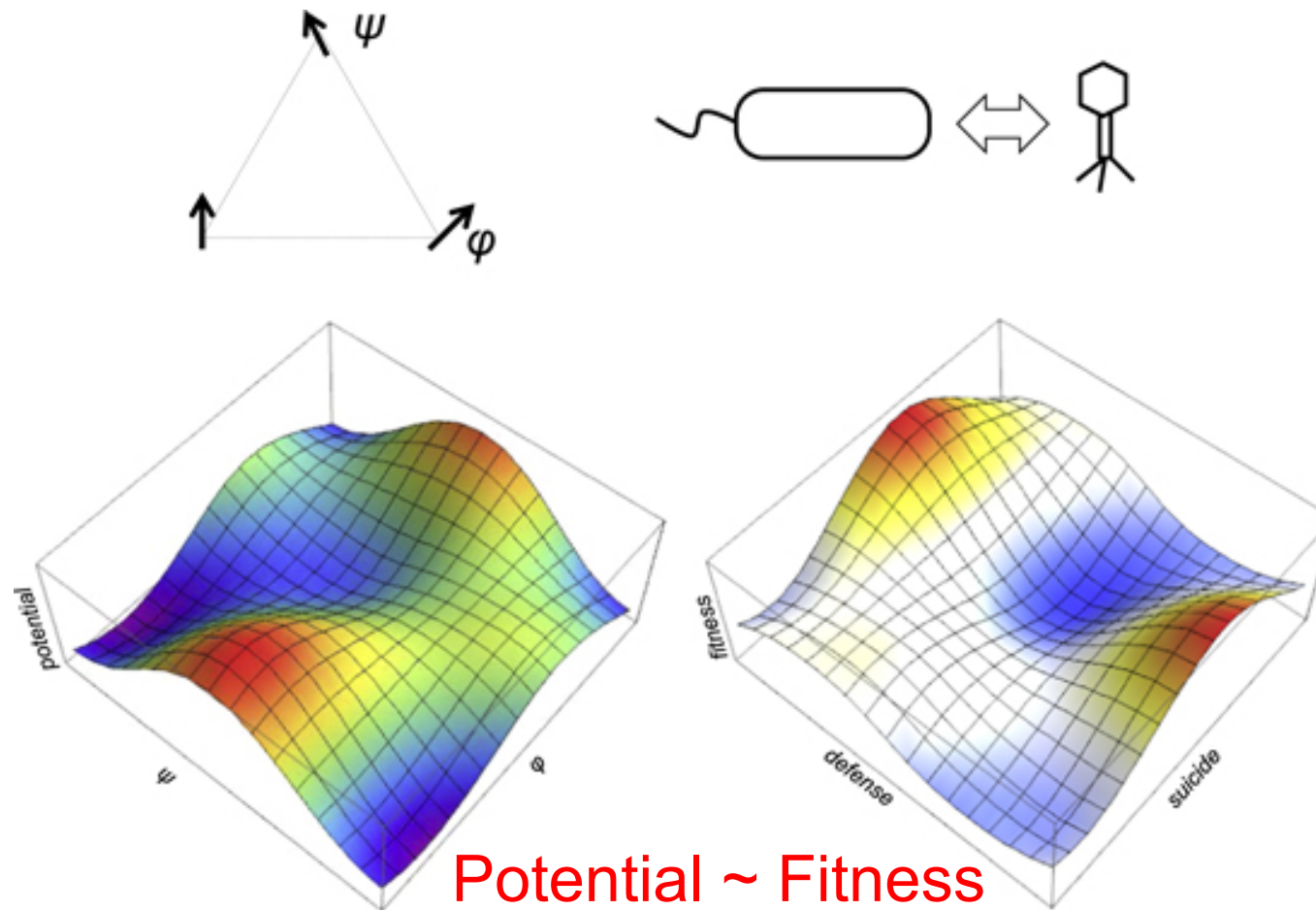


**Clusters,
suicide**



**Under strong pathogen pressure, suicide/multicellularity
provide the only path to high fitness**

Competing interactions and frustration in physical and biological systems



Competing interactions drive evolution of complexity: from simple glass-like materials to biological systems

Wolf, Katsnelson, Koonin. Physical foundations of biological complexity. PNAS 2018 in press
<https://arxiv.org/abs/1803.09975>

Competing interactions and frustrated states in biology

System	Frustration-producing elements (competing interactions)	Evolutionary consequences
Proteins	Hydrogen and Van der Waals bonds between side chains of monomers	Emergence of stable conformations and semi-regular patterns in protein structures
Gene regulation networks	Activators and repressors	Emergence of meta-stable expression patterns
Cells	Membranes and channels	Emergence of compartments and cellular machinery dependent on electrochemical gradients
Autonomous and semi-autonomous self-replicating genetic systems	Replicator and parasite genomes	Emergence of self vs nonself discrimination
Autonomous and semi-autonomous self-replicating genetic systems	Host cells and viruses	Emergence of infection mechanisms, defense and counter-defense systems, evolutionary arms race
Autonomous and semi-autonomous self-replicating genetic systems	Host cells and transposons	Emergence of intra-genomic DNA replication control; hotbeds of evolutionary innovation
Autonomous and semi-autonomous self-replicating genetic systems	Host cells and plasmids	Emergence of beneficial cargo genes, plasmid addiction systems, efficient gene exchange and transfer mechanisms

Competing interactions and frustrated states in biology

Communities of unicellular organisms	Individual cells	Emergence of information exchange and quorum sensing mechanisms; replication control apoptosis and multicellularity
Multicellular organisms	Soma and germline	Emergence of complex bodies and sexual reproduction
Populations	Individual members	Emergence of population-level cooperation; kin selection
Populations	Partners with unequal parental investment (males and females)	Emergence of sexual selection and sexual dimorphism
Biosphere	Species in different niches	Emergence of interspecies competition, host-parasite and predator-prey relationships, mutualism
Societies

Conclusions

- Inevitability of parasites in all evolving replicator systems: **genetic parasites as a universal of life**
- Inevitable parasite persistence to escape Muller's ratchet
- Host-parasite conflicts drive evolution of complexity including **major evolutionary transitions**
- **Competing interactions and frustrated states**, analogous to those in theory of striped glasses: a key factor of evolution central to emergence of complexity – in biology and beyond

Contributors



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