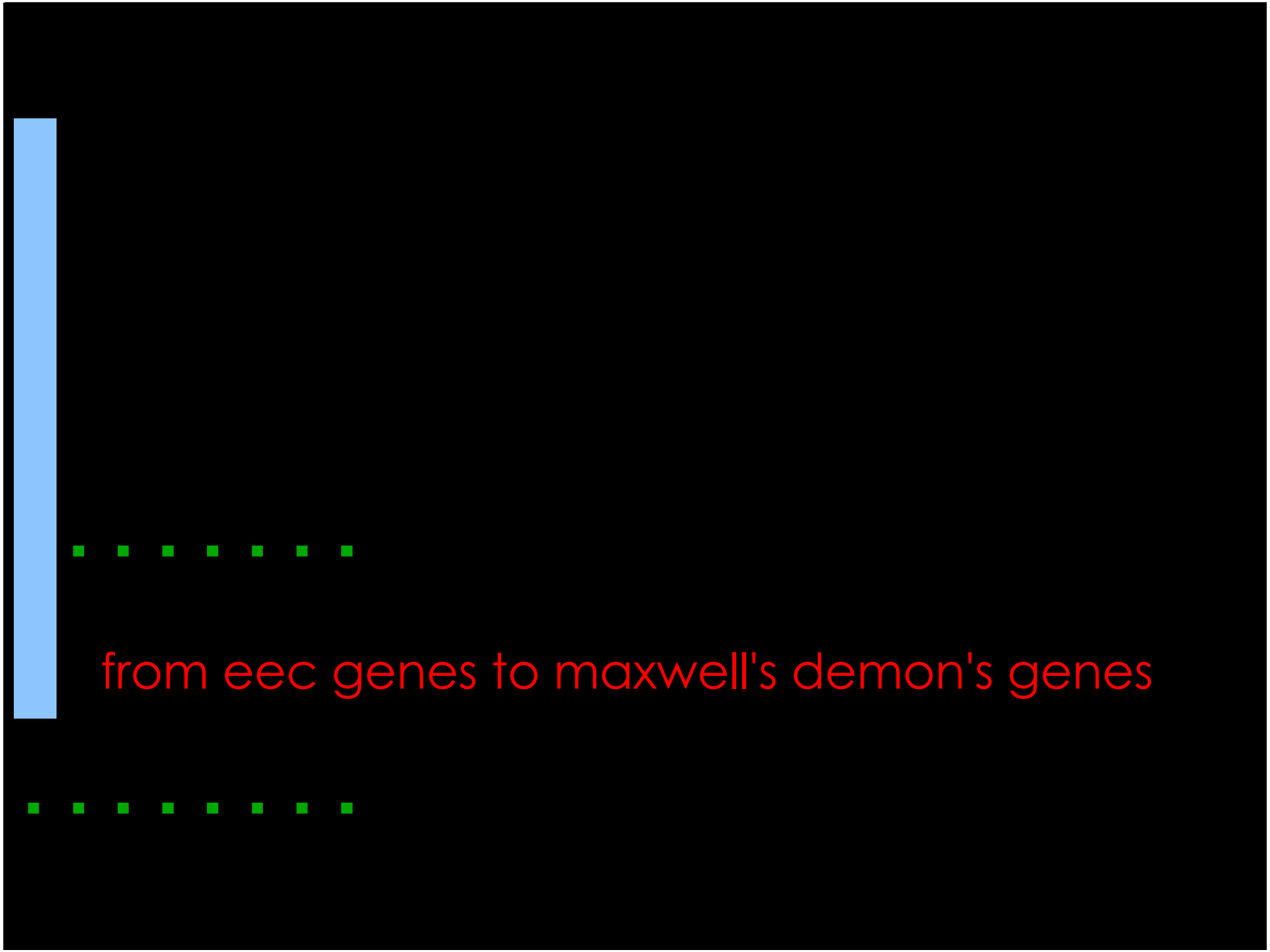

from eec genes to maxwell's demon's genes

antoine danchin 唐善・安東

AMAbiotics SAS

piotr slonimski, from mitochondria to genomes
gif sur yvette, july 8, 2010

eec meeting, elounda, crete, may 1991

in 1991, europe was pioneering microbial genomics with two programmes supported by the european commission: sequencing of the genomes of *saccharomyces cerevisiae* and *bacillus subtilis*

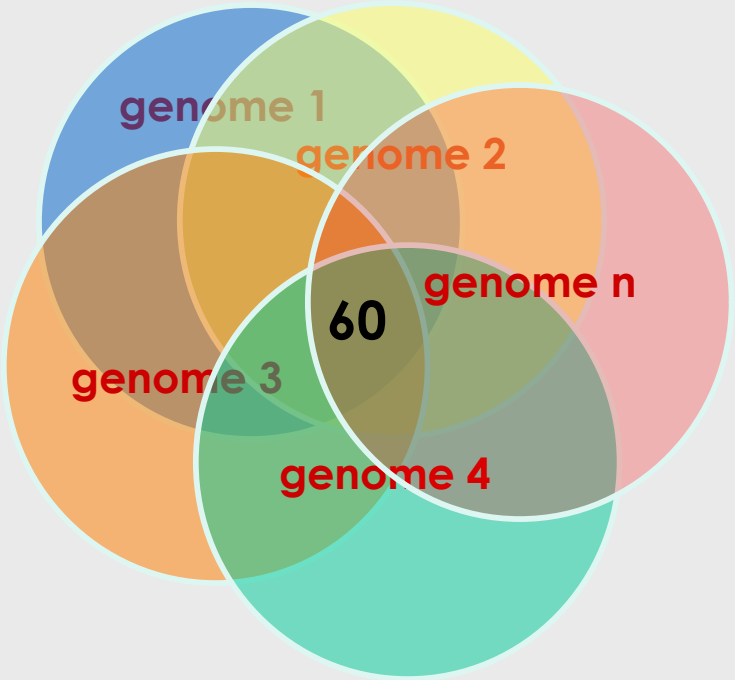
at the elounda meeting, the first discovery of genomics was presented: the sequence of yeast chromosome III and 100 kb of the genome of *b. subtilis* revealed that > 50 % of the cds did not look like anything known yet; this was a complete surprise as the adversaries of the genomic programmes argued that nothing unknown would be discovered

piotr slonimski proposed to name these genes "elusive, esoteric, conspicuous" genes, eec genes, to celebrate the support of the eec

a minimal set of functions

. . . . . .

2003: 60 conserved proteins



the number of conserved genes tends to zero!

from functional ubiquity to gene persistence

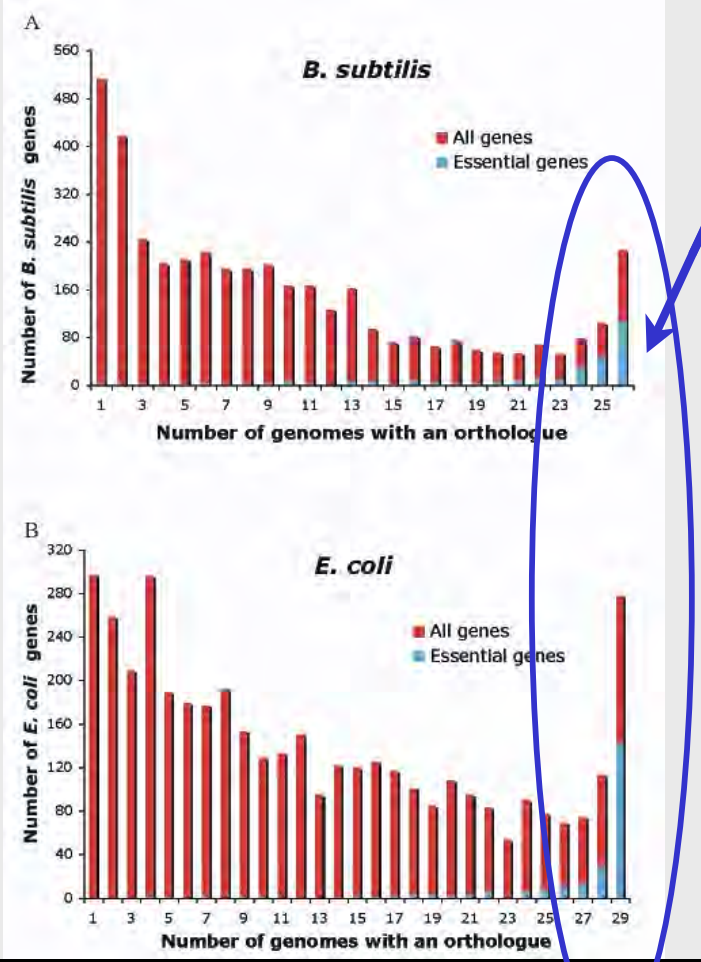
functional gene ubiquity does not imply gene ubiquity;
yet, efficient entities tend to persist through generations

- looking for « persistence » identifies most ubiquitous functions

~ 500 genes persist in bacterial genomes; they are involved not only in the three processes required for life but also in maintenance and adaptation to transient phenomena ; a fraction manages the evolution of the organism

a common structural feature: persistent genes are located in the leading DNA strand

is « ubiquitous » synonymous with « essential »?



persistent genes

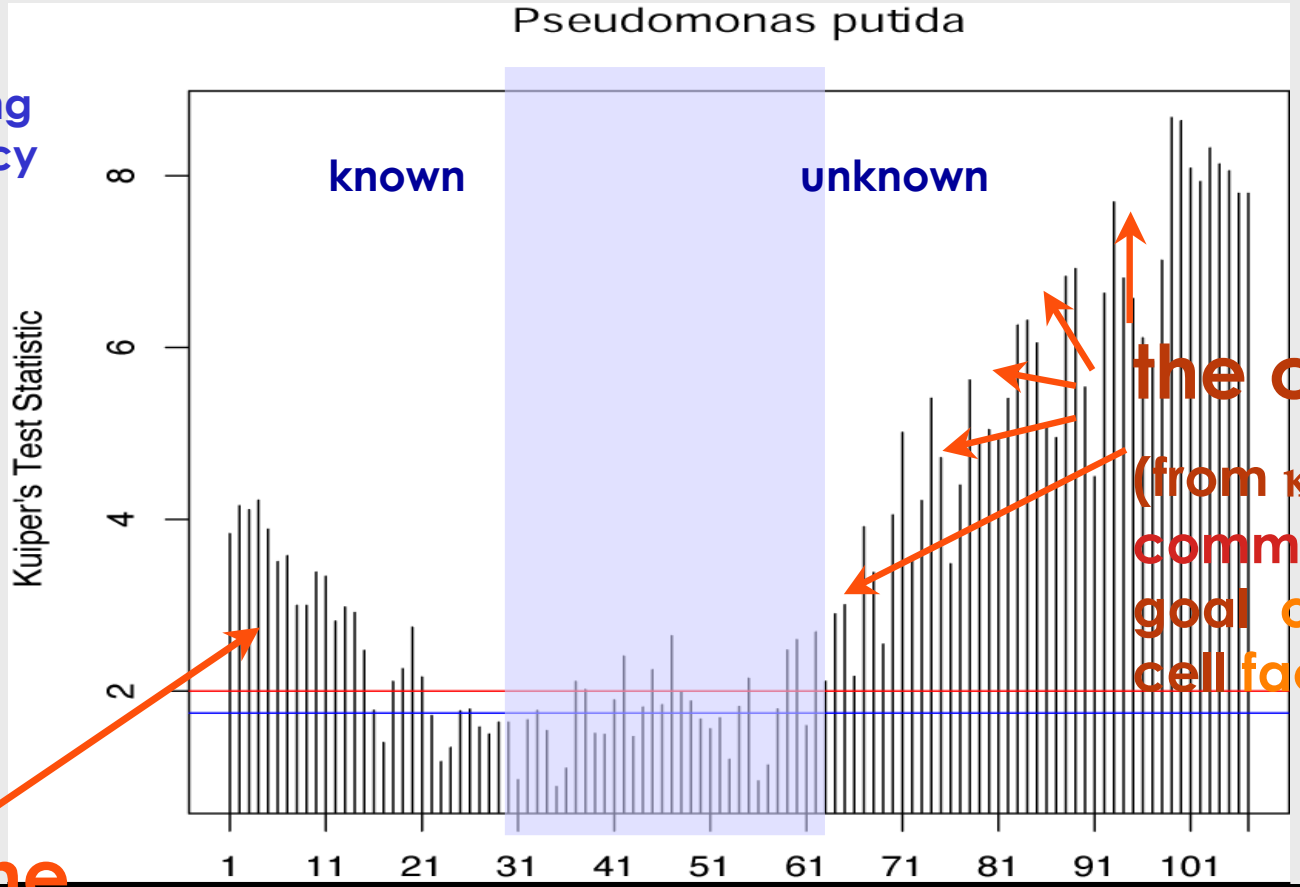
genes essentiels and ….

too many genes!

energy-dependent degradation
metabolic patches

g fang, ep rocha, a danchin
how essential are non-essential genes?
mol biol evol (2005) 22: 2147-2156

organisation of bacterial genomes



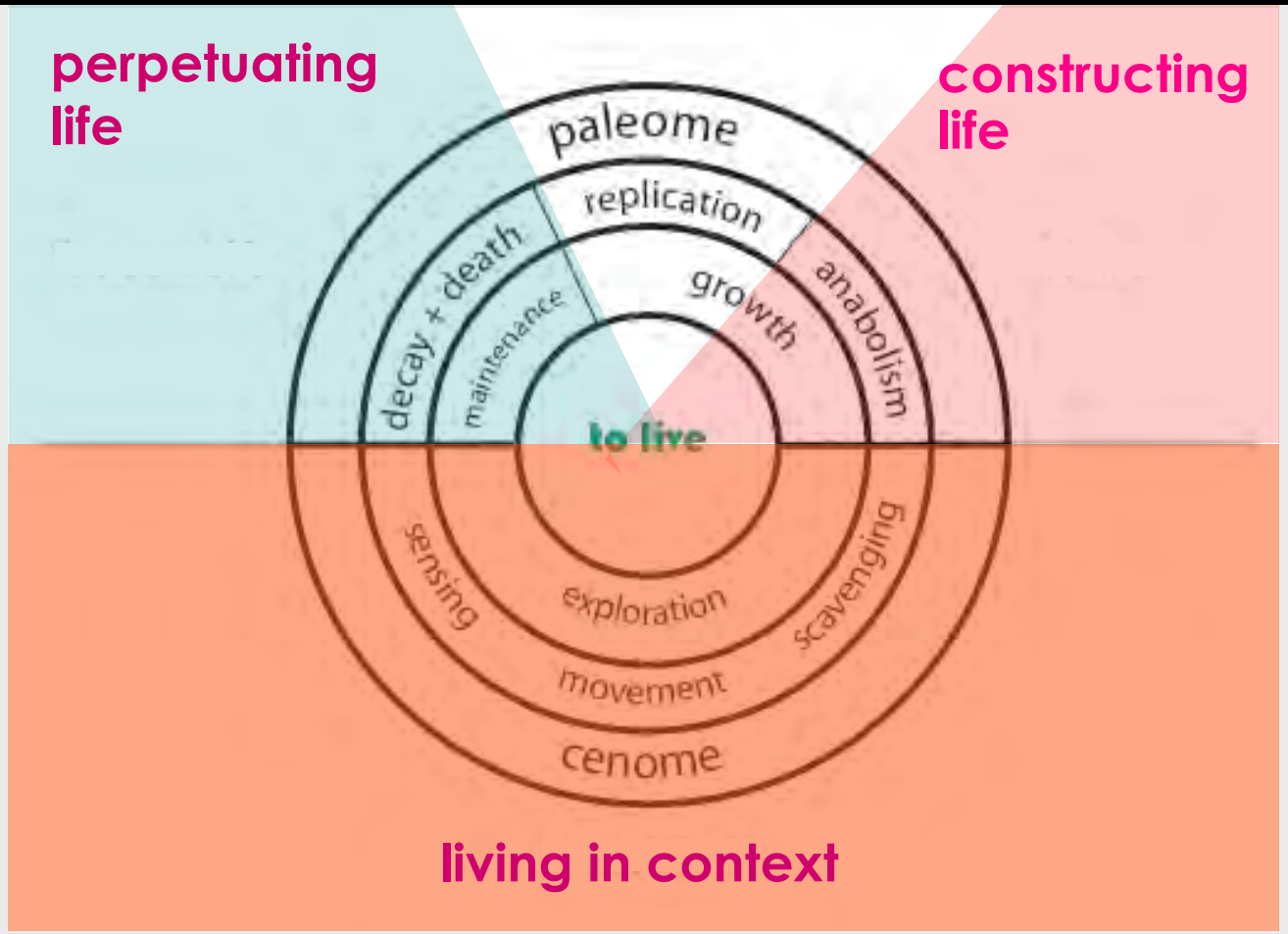
the cenome

(from κοινος, common): the goal of the cell factory

paleome

(from παλαιος, ancient): the cell factory

a tale of two genomes



organised genome dynamics in the *escherichia coli* species results in highly diverse adaptive paths
touchon m, hoede c, tenaillon o, barbe v, ..., medigue c, rocha ep, denamur e.
plos genet. 2009 jan;5:e1000344

maxwell's demon's genes

cells and computers

genetics rests on the description of genomes as texts written with an alphabet: but do cells behave as computers?

horizontal gene transfer

viruses

genetic engineering

transplantation of a naked genome in a recipient cell changing the host recipient into a new one (2007)

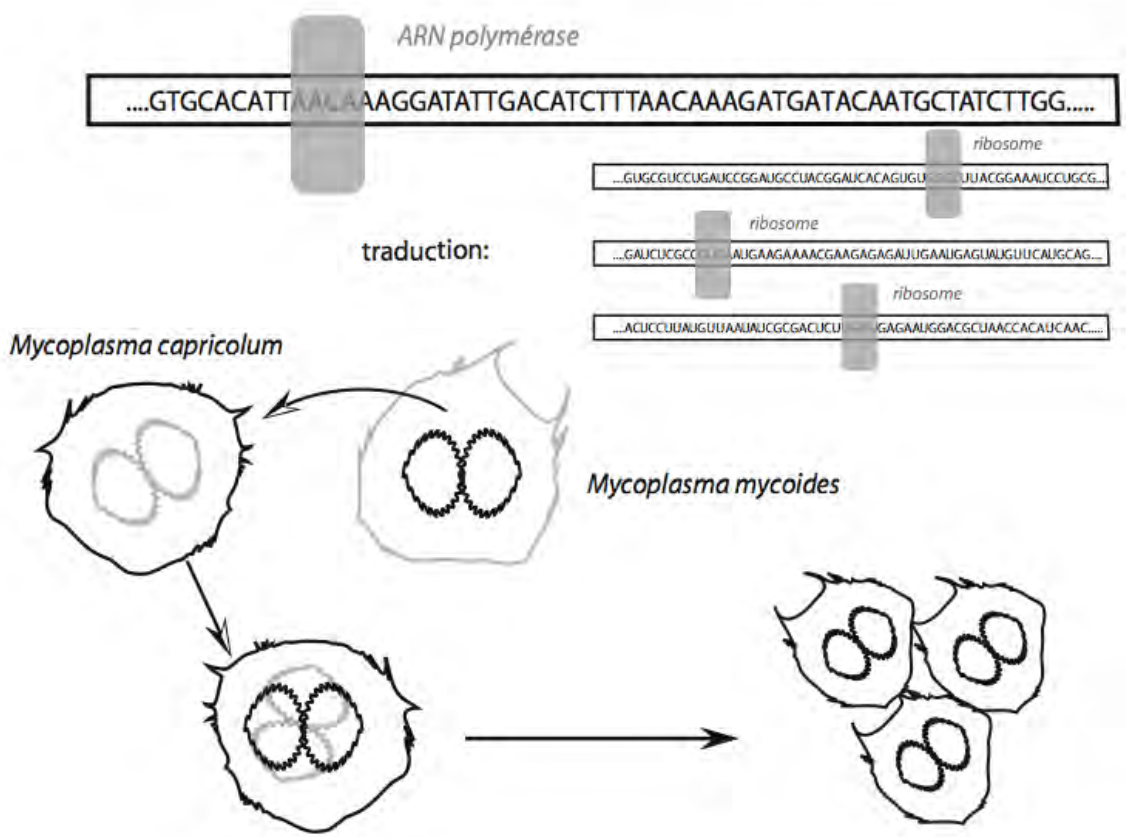
everything separates

"machine" (cell factory) and "data/program" (genome)

cells as turing machines

the turing machine

genome transplantation



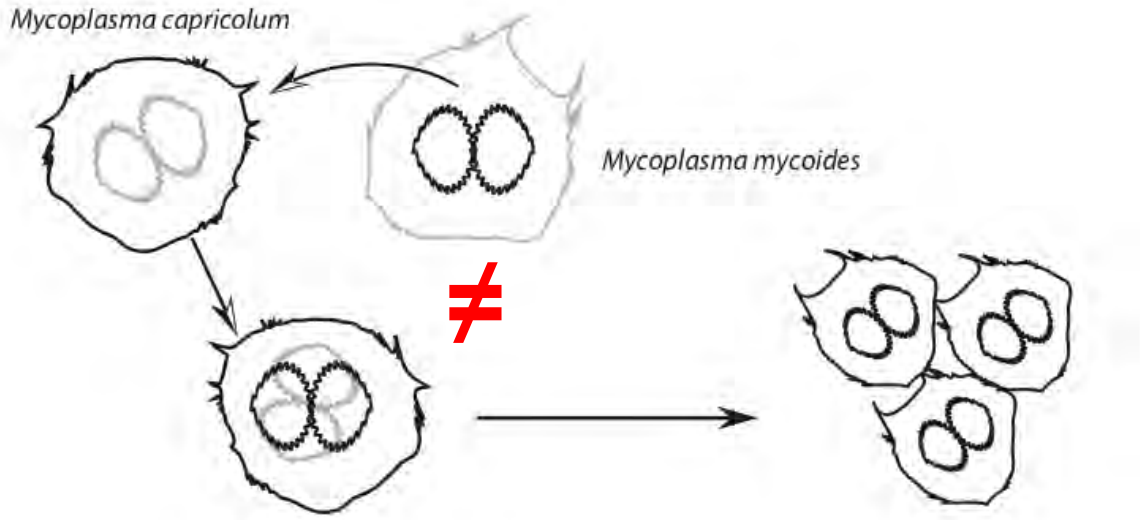
genome transplantation in bacteria: changing one species to another
lartigue c, glass ji, alperovich n, pieper r, parmar pp, hutchison ca 3rd, smith ho, venter jc
science (2007) 317: 632-638

caveat: reproduction vs replication

the program replicates (makes an identical copy)

the cell reproduces (makes a similar copy)

this split is the basis of evolution



babies are born very young!

the machine reproduces

reproduction can improve over time: it is always an old organism that gives birth to a young one (this implies creation and accumulation of information)

the program replicates

replication progressively accumulates errors

which genes permit accumulation of information?

revisiting information

intuition tells us that creation of information asks for energy

wrong: creation of information is reversible (landauer, 1961; bennett, 1982, 1988, zurek, 1989); yet, to accumulate information requires an energy-dependent processs to "make room", without erasing valuable information

open question:

can we identify in genomes the genes coding for the functions that permit this process?

can we find a ubiquitous and stable energy source?

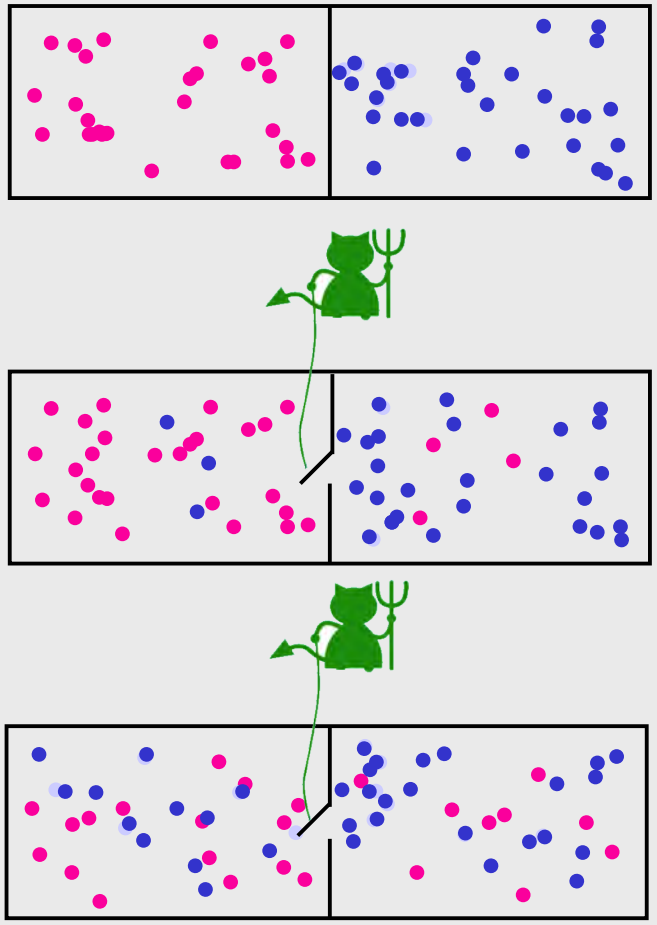
value of information

classical models of information do not take "meaning" into account, nor the value of an information

the information of the program is transmitted "as is" during replication, with no value associated to particular sequences: where does the information of the machine come from?

can we imagine the genes of a maxwell's demon which would select among what is functional or young (locally) and what does not work?

maxwell's demon



the demon accumulates information or reverses time if it can measure the speed and the position of the atoms of gas, collecting an information to calculate when it must close the trap

0

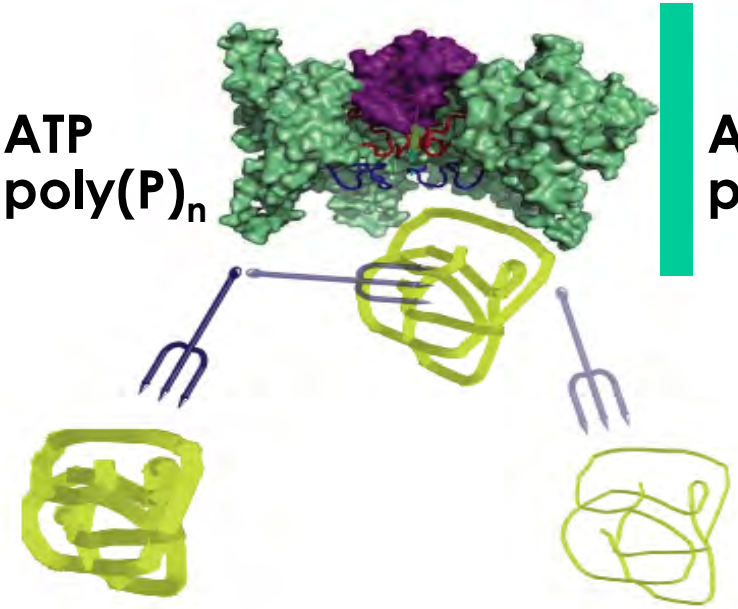
t

0

t

maxwell's demon's genes

ATP
poly(P)$_n$



ADP + Pi
poly(P)$_{n-1}$ + Pi **<= in the paleome**

the degradation machinery uses energy to reject unaltered a functional entity

non functional entities are recognised and degraded

innovation: adaptive mutations

- energy-dependent accumulation of information is blind; it ignores the source of information
- information can come from a memory, that of the pre-existing genome; it can also be created de novo

- adaptive mutations are de novo creations of information; therefore they dependent on genes involved in accumulation of information

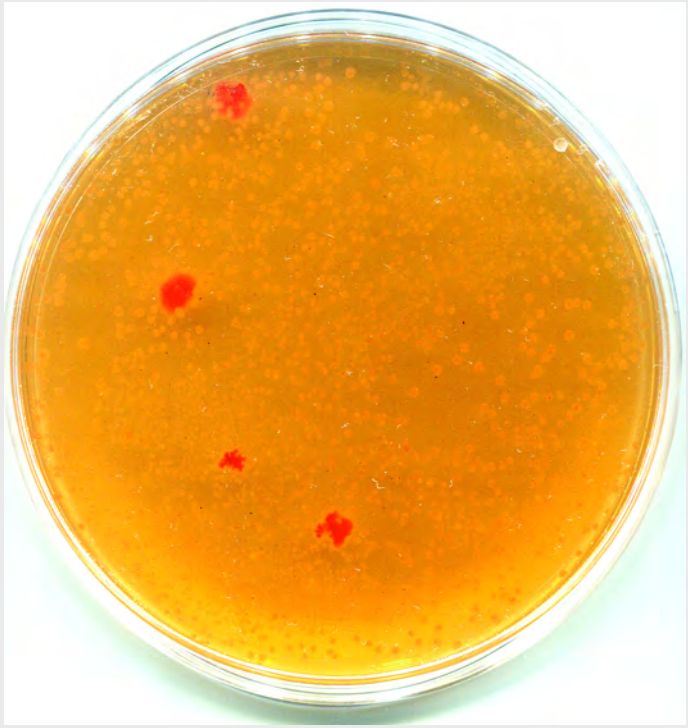
adaptive mutations

construction of "intelligent" bacteria

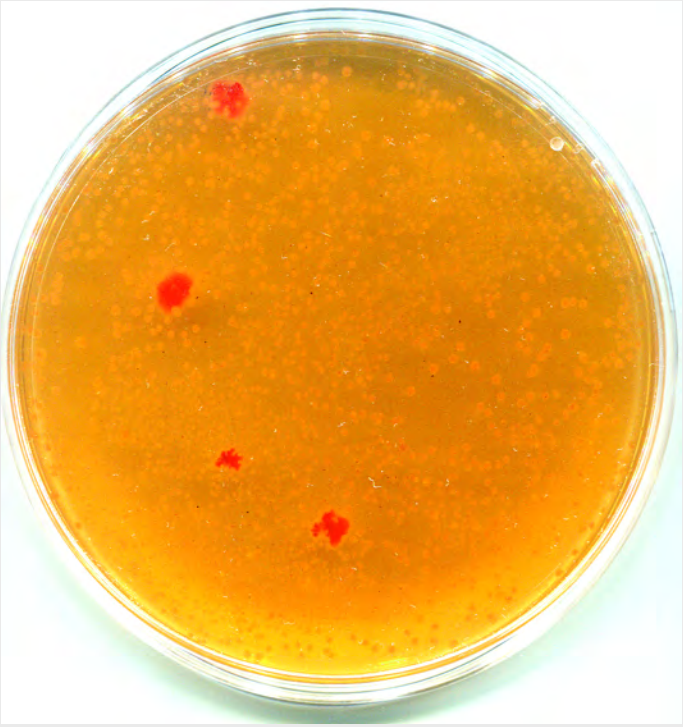
placed to grow on a medium with limited nutrient supply; form colonies of approximately 10^7 bacteria; the medium also contains nutrients that they cannot use

after a few weeks time, papillae appears that begin to grow and invade the medium, using supplied "unusable" nutrients; they derive from adaptive mutations

they did not pre-exist, and this supposes creation of information



adaptive mutations



sequencing seven genomes + 30 pcrs

the total number of mutations is higher in older colonies

mutations are spread throughout the chromosome, and concentrated in one gene => pcr of many colonies

in this particular gene one finds different mutations in different papillae, 2 mutations in 30% of the cases

in some cases one of the two mutations is silent

on a particular carbon source, there is a least one other gene involved

natural selection is a principle of physics

- **natural selection**: making room using energy to avoid erasing context-dependent functional information
- energy-dependent degradative processes make room for newly synthesised entities; energy is consumed to **prevent** degradation of functional entities
- this process accumulates information, whatever its origin, in a ratchet-like process
- this process is **myopic**: it cannot have a design, hence the "tinkering" feature of life and its evolution

predictions

- bacterial persistence in a host depends on persistent non-essential genes
- initiation of cancer comes from cells (stem cells) that discovered adaptive mutations that permit them to generate an immortal progeny
- accumulation of information in the brain (memory and learning) implies the existence of processes to make room while preserving functional connections, in a way which must be energy-dependent

a synthetic cell?

- the engineering view of SB precludes that artificial cells be innovative
- we can exclude the genes permetting accumulation of information
- the consequence is that the cell factory will age and will need to be systematically rebuilt
- this has a in-built societal benefit, as risks are minimised
- but this poses problems when applications require that industrial processes are scaled-up: this may not be possible, unless we can harness the function of the maxwell's demon's genes to the human goals

contributions

in silico

gang fang, eduardo rocha

in vivo

agnieszka sekowska, evelyne turlin, andrew martens

collaborations

genoscope, beijing genome institute, fudan university, the university of hong kong, hong kong university of science and technology