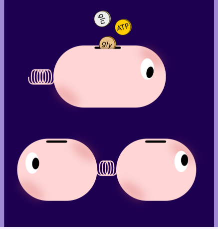

Growth in uncertain environments

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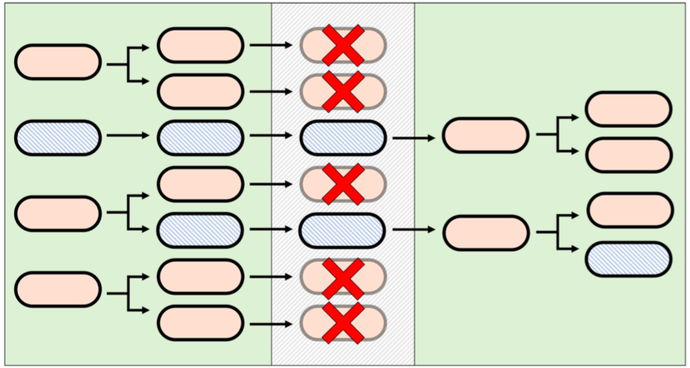
Introduction

Bacterial persistence: experiments

Bacterial persistence: elementary model



- 2 states R: growing (R=1) / dormant (R=0)
- 2 environments E: antibiotics (E=+) / no antibiotics (E=-)
- multiplication factor in one generation f(R,E)

	E = -	*E* = +
R = *0*	1	1
R = *1*	0	2

- probability for antibiotics (E=+) : p
- probability to be dormant (R=0): u

(drawn at each generation)

Question: given f(R,E) and p, optimal transition rate u ?

Meta question: optimal in what sense?

Bacterial persistence: elementary model

Two limits: (1) Large population
(2) Long time

(1) Given Nt cells at generation t, fraction u of cells with R=0 (dormant), 1-u with R=1 (growing)

If no antibiotics (E=+): $N_{t+1} = A_+ N_t$ $\quad A_+ = u + 2(1-u) = 2 - u$

If antibiotics (E=-): $N_{t+1} = A_- N_t$ $\quad A_- = u$

(2) Over T generations, fraction p of generations with E=- (antibiotics), fraction 1-p with E=+ (no antibiotics)

$$N_T = (A_-)^{pT} (A_+)^{(1-p)T} N_0$$

$$N_T = e^{\Lambda T} N_0$$

$$\Lambda = p \ln A_- + (1-p) \ln A_+$$
$$= p \ln u + (1-p) \ln(2-u)$$

$$u = \begin{cases} 2p \;, & \text{if } 0 < p \leq 1/2. \\ 1, & \text{if } 1/2 < p \leq 1. \end{cases}$$

Conclusion: optimal transition rate u adapted to the uncertainty p of the environment

General model with sensing

- n states R
- M environments E, probability p(E)
- multiplication factor f(R,E)
- switching probability u(R|S) where S is a cue (previously just u(R), recovered if S is independent of E)
- probability q(S|E) for S given E

Muliplicative factor given E,S: $N_{t+1} = A(E,S)N_t$ $$A(E,S) = \sum_R f(R,E)u(R|S)$$

Growth rate: $$\Lambda = \sum_{S,E} q(S|E)p(E)\ln A(S,E)$$

Geometric mean $\Lambda = \langle \ln A(S,E) \rangle_{S,E}$ not arithmetic mean $\Lambda = \ln \langle A(S,E) \rangle_{S,E}$

Arithmetic vs geometric means

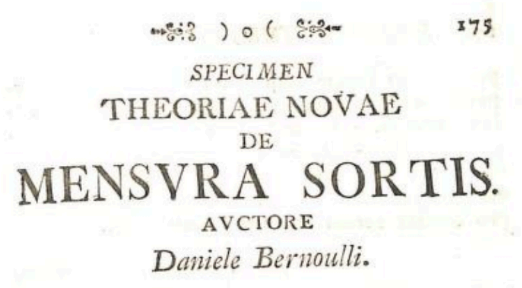
Growth is not an additive but a multiplicative process!

Didactic example:

A=2 with p=1/2 or A=1/3 with p=1/2

arithmetic mean = (1/2)(2+1/3) > 1

geometric mean = (2*1/3)^(1/2) < 1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SPECIMEN
THEORIAE NOVAE
DE
MENSVRA SORTIS.
AVCTORE
Daniele Bernoulli.

D Bernoulli, Exposition of a new theory on the measurement of risk (1738)

Back to the simple model of bacterial persistence:

optimal geometric mean: u =

optimal arithmetic mean: u = 0 — very risky strategy that leads to extinction if E=- even occur!

Value and cost of information

$$\Lambda = \sum_{S,E} q(S|E)p(E)\ln A(S,E) \qquad A(E,S) = \sum_R f(R,E)u(R|S)$$

Without sensing and with f(R,E)=f(E)delta (R,E) (Kelly case, see 2nd part)

$$\Lambda = \sum_E p(E)\ln(f(E)u(E)) = \sum_E p(E)\ln f(E) + \sum_E p(E)\ln p(E) - \sum_E p(E)\ln(p(E)/u(E))$$

Value of sensing, again with f(R,E)=f(E)delta (R,E)

With no sensing, i.e. S independent of E, optimal growth rate

With sensing, i.e. given q(S|E), optimal growth rate

Value of sensing: $\Lambda^*(q) - \Lambda^*(\emptyset) = \sum_{S,E} q(S|E)p(E)\ln q(S|E)$

Biologically, also a cost c(q) that increases with precision => a trade-off and optimal sensor

Analogies with financial investment

Biology	**Finance**
Individual	Currency unit
Environment $p(E)$	Market state
–	Investor
Phenotype decisions $u(R)$	Investment strategy
Multiplicative rate $f(R,E)$	Immediate return
Environmental cue $P(S\|E)$	Side information

Major difference: information is centralized in finance, distributed in biology

Implication: one sensor per cell, heterogeneity that is beneficial

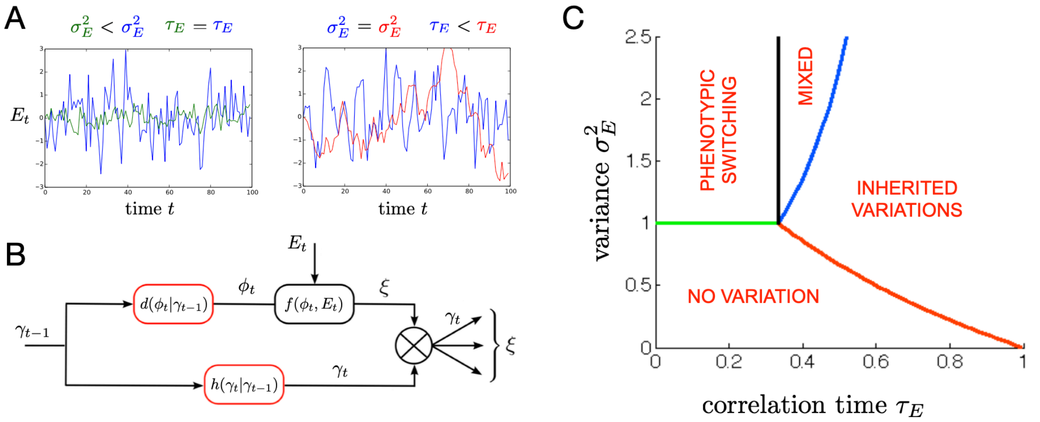
$$\Lambda = \sum_{S,E} q(S|E)p(E) \ln A(S,E) \quad < \quad \Lambda = \sum_{S,E} p(E) \ln A(S,E) q(S|E)$$

Warning: what is optimal for a population may not be evolutionary stable!

Conflict between levels of selection!

Optimal strategies in correlated environments

Heredity: passing information between generations



Summary and perspectives

Short/intermediate times and finite population: see David