Exponential Growth or Death?

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Malthus's Law:

"A population, when unchecked, increases in a geometrical ratio. Subsistence increases only in an arithmetical ratio. A slight acquaintance with numbers will shew the immensity of the first power in comparison of the second."

(*An Essay on the Principle of Population as it Affects the Future Improvement of Society...*, 1798)

Growth or Extinction:

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- I. J. Bienaymé (1845) and F. Galton (1873).

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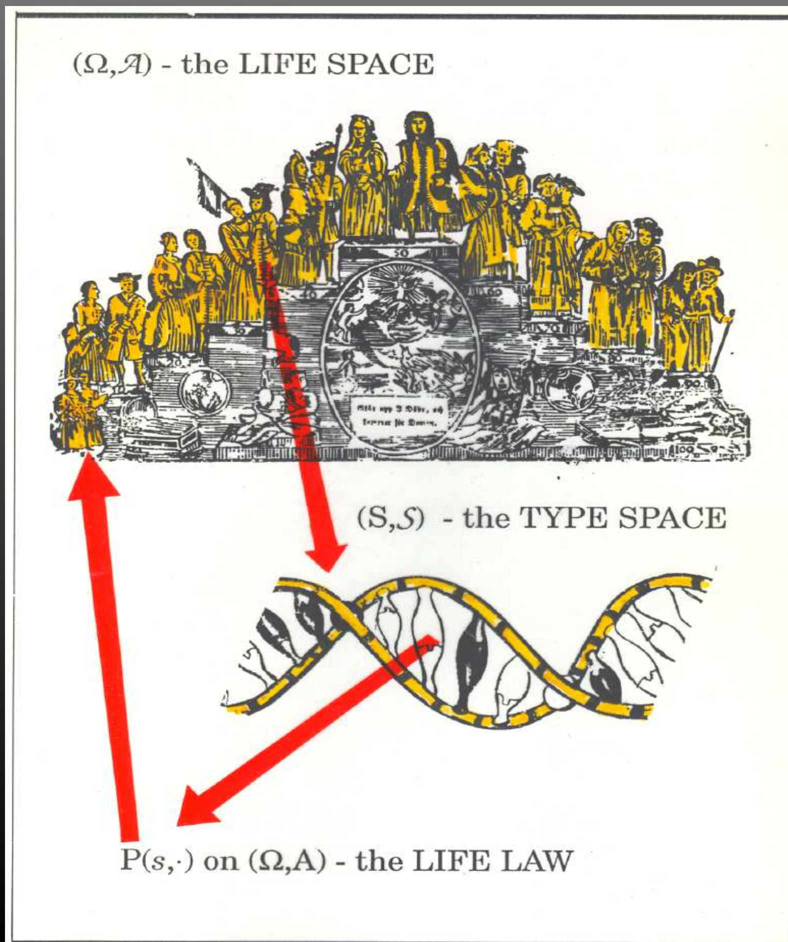
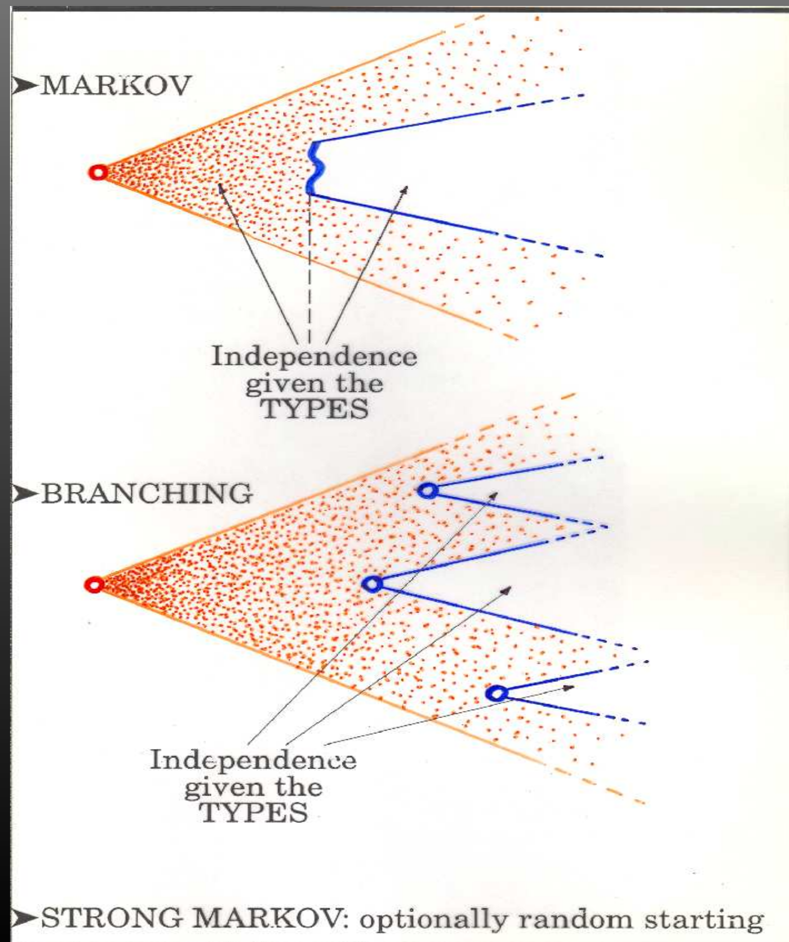
- Individual reproduction is any point process over (mother's) age $\times$ (child's) type.

The Markov and Branching Properties





What if a population is “checked”?

Consider non-negative $X_1, X_2, \ldots$ such that $X_n = 0 \Rightarrow X_{n+1} = 0$. Suppose that there is a history-independent risk of extinction:
For any x there is a $\delta > 0$ such that

$$\mathbf{P}(\exists n; X_n = 0 \mid X_1, \ldots X_k) \geq \delta,$$

if only $X_k \leq x$. Then, with probability one either

- there is an n such that all $X_k = 0$ for $k \geq n$ or
- $X_k \to \infty$ as $k \to \infty$.

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- In all these cases the dichotomy holds.

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- The general case remains.

Simple Processes in General Environments

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- Population size is part of the environment, $Z_n \in \mathcal{E}_n$
- Reproduction probabilities are determined by $\mathcal{E}_n$.
- Given $\mathcal{E}_n$, individuals reproduce independently (and according to the same distribution – single type).

Near Critical Reproduction

Write μ_n for the expected offspring per individual, given $\mathcal{E}_n$, Assume $\mu_n = 1 + C_n/Z_n + R_n$, if $Z_n > 0$. C_n independent of Z_n, $R_n = o(1/Z_n)$.

- Then, with $R_n = 0$,
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- With $c_n = \mathbf{E}[C_n]$, independence yields
  $\mathbf{E}[Z_N] = \mathbf{E}[Z_0] + \sum_{n=1}^{N} c_n\mathbf{P}(Z_n > 0)$.

Asymptotics

- With $\mathrm{P}(Z_n > 0) \to \mathbf{P}(Z_n \to \infty) = 1 - q > 0$,

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- What about the process itself,

$$Z_N / \sum_{1}^{N} c_n \sim ?$$

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- Improving outer environment (like $c_n \sim cn$)

$$Z_N \sim cN^2/2.$$

Process Convergence – Assumptions:

(1) The conditional offspring distributions at times $n = 0, 1, 2, \ldots$, possess moments of all orders. For each order, these are bounded above;
(2) $\sum_{j=1}^{n} c_j \to \infty$ and $c_n / \sum_1^n c_j \to 0$;
(3) Reproduction variances σ_n^2 stabilise as the population grows: $\sigma_n^2 \to V_n, \mathbf{E}[V_n] = v_n$, V_n (like C_n) independent of Z_n.

(4) Reproduction variances do not swamp means:

$v_n \sim ac_n, a \geq 0$.

Process Convergence — Conclusion:

Then, either the population goes extinct or

$$\frac{Z_n}{\sum_{j=1}^{n} c_j} \xrightarrow{d} \Gamma(\frac{2}{a}, \frac{2}{a}),$$

where $\Gamma(\infty, \infty) = 1$.

Proof by the method of moments and induction:

$$\mathbf{E}[Z_{n+1}^k | \mathcal{E}_n] = Z_n^k + \left(kC_n + \binom{k}{2} V_n \right) Z_n^{k-1} + o(Z_n^{k-1}).$$

PCR

The *Polymerase Chain Reaction*, generates a test sample out of a minuscule amount of DNA. In *quantitative* PCR the successive growth of the amount of DNA is followed from a threshold of observation up to large molecule numbers. In ordinary PCR focus is on the end product, which is sufficiently big to detect viruses or mutations, and for paternity testing or forensic matters.

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- Temperature is raised and an enzyme, the *polymerase* promotes the synthesis process at the region marked by the primers, the primer extending into a complementary DNA string.

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- After an unclear beginning, *exponential* growth,
- followed by *linear* increase,
- gradually changing over into *saturation*.

Model

$$\#\text{ “offspring”} = \begin{cases} 2 & \text{with probability } p \\ 1 & \text{with probability } 1-p \end{cases}$$

In most literature, $p = 1$ – or constant. But $p = p$(target DNA, primers, Taq polymerase, deoxinucleic triphosphate, $MgCl_2 \ldots$).

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- By classical enzyme kinetics, the rate of the reaction is $z/(z+K)$, where K (very large) summarises all other influences.
- Thus, in one cycle starting from z, $zp(z) \propto z/(z+K)$ new molecules are synthesized.

PCR is near-critical

Since $p(1) \approx 1$, $p(z) = \frac{K}{K+z}$. Let K_n be the Michaelis Menten constant in the n:th cycle. Then,

$$\mu_n = 1 + \frac{K_n}{K_n + Z_n} = 1 + K_n/Z_n + o(1/Z_n)$$

and

$$\sigma_n^2 = \frac{K_n Z_n}{(K_n + Z_n)^2}.$$

and grows linearly:

If the M-M constants have the same mean,

$$c_n = \mathbf{E}[K_n] = c, \text{ then } \sum_1^n c_j = cn,$$

and $v_n = o(1)$, so that

$$Z_n/n \to c$$

in probability.

The Martingale

Doob: $Z_{j+1} = \mu_j Z_j + Z_{j+1} - \mathbf{E}[Z_{j+1}|\mathcal{E}_j] = Z_j + \frac{K_j Z_j}{K_j + Z_j} + Z_{j+1} - \mathbf{E}[Z_{j+1}|\mathcal{E}_j]$. Repeat to obtain $Z_n = Z_0 + A_n + M_n$, where

$$A_n = \sum_{j=0}^{n-1} \frac{K_j Z_j}{K_j + Z_j}$$

is increasing and in $\mathcal{E}_{n-1}$. Since $Z_j \to \infty$, $A_n/n \to c$ a. s., by LLN, eg. if the K_j are i.i.d.

Almost sure convergence

$M_n = \sum_{j=1}^n Z_j - \mathbf{E}[Z_j|\mathcal{E}_{j-1}]$ – a martingale with respect to $\{\mathcal{E}_n\}$.

$$\mathbf{E}[(M_n - M_{n-1})^2|\mathcal{E}_{n-1}] = \text{Var}[Z_n|\mathcal{E}_{n-1}] =$$

$$= \frac{K_{n-1}Z_{n-1}^2}{(K_{n-1} + Z_{n-1})^2} \leq K_{n-1}.$$

Hence, $\sum_{n=1}^\infty \mathbf{E}[(M_n - M_{n-1})^2]/n^2 < \infty$.

Almost sure convergence

Since $\sum_{n=1}^{\infty} \mathbf{E}[(M_n - M_{n-1})^2]/n^2 < \infty$. the Martingale Law of Large Numbers yields $M_n/n \to 0$ a. s. Hence,

$$Z_n/n = Z_0/n + A_n/n + M_n/n \to 0 + c + 0,$$

with probability one.

Linear growth

This recovers the linear phase of quantitative PCR. Saturation requires a more subtle discussion of K_n when Z_n or $n \to \infty$.

Joint work with F. C. Klebaner. Partly published in J. Appl. Prob 41 (A), 2004.