Growth of Population in Catastrophic Environments

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Summary

- Phase variation and ‘bet hedging’
- Model system of catastrophes:
  Piecewise deterministic Markov Process
- Exact stationary distribution of ‘fitness’
- Optimal strategies for growth

Phase variation

- Populations of cells (especially bacteria) are very heterogeneous even if environmentally and genetically identical

- This may be important in surviving stresses coming from environment
  it is called phase variation
  (e.g.: fimbriae on E. coli bacteria)

- How can a population be heterogeneous in gene expression?
  $\Rightarrow$ "genetic switches"

Examples of phase variation

"Once and for all" – Population splits into groups with long lived phenotypes i.e. bistability

"bet hedging" – small fraction of population in unfit "persistor state" which can survive catstophes e.g. antibiotics

Defence against immune response – small fraction of population in fit state since too successful a population would evoke an immune response

General scenario

- Population of bacteria, say, with two possibles states for individuals:

  Fit state has fast growth
  Unfit (persistor) state has slow growth but withstands catastrophes

- **Catastrophes** occur stochastically, coupled to growth of population

- **Question:** what is best 'strategy' of population to maximise growth?

Model

1 Deterministic growth:

Two subpopulations n_A and n_B.

Exponential growth rates $\gamma_A > \gamma_B$

Individuals switch states with rates k_A, k_B

$$\frac{\mathrm{d}n_A}{\mathrm{d}t} = \gamma_A n_A + k_B n_B - k_A n_A \, ,$$

$$\frac{\mathrm{d}n_B}{\mathrm{d}t} = \gamma_B n_B + k_A n_A - k_B n_B \, .$$

2 Stochastic catastrophes:

Catastrophe rate $\beta(n_A, n_B)$ *environmental response function*

When a catastrophe occurs $n_A \to n'_A < n_A$, with probability density $\nu(n'_A | n_A)$.

Fitness

Biological definition: instantaneous growth rate of population

Here f is fraction of population in fit state

$$f = \frac{n_A}{n_A + n_B}$$

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \gamma_A n_A + \gamma_B n_B = (\gamma_B + \Delta\gamma f)n$$

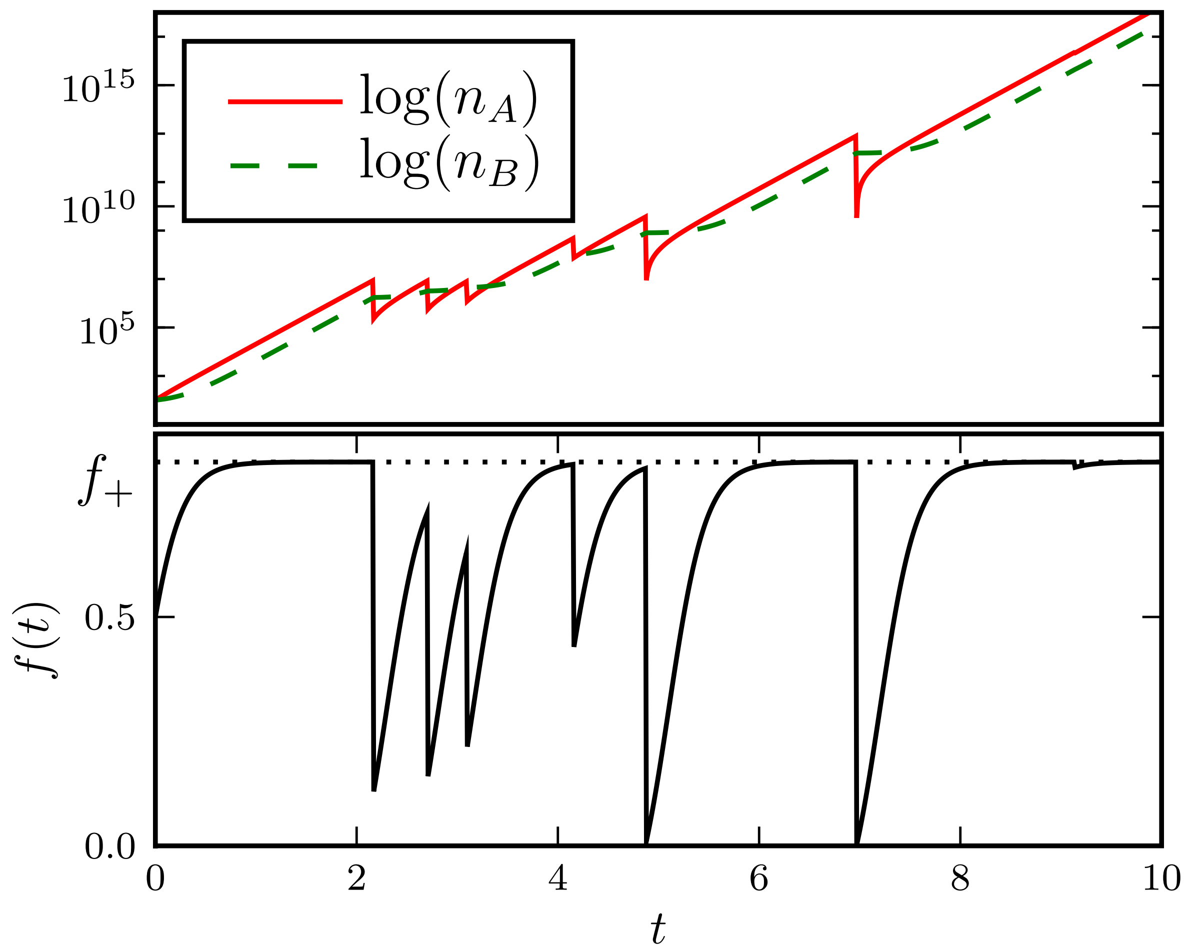
Deterministic growth:

$$\frac{\mathrm{d}f}{\mathrm{d}t} = v(f) = \Delta\gamma(f_+ - f)(f - f_-) \ ,$$

where $f_\pm$ are the roots of

$$f^2 - \left(1 - \frac{k_A + k_B}{\Delta\gamma}\right) f - \frac{k_B}{\Delta\gamma} = 0 \ .$$

Typical trajectory



Piecewise Deterministic Markov Processes

M. H. A. Davis
Piecewise-deterministic Markov processes: a general class of non-diffusion stochastic models,
J Royal Statist Soc (B) 46 (1984) 353-388

Used extensively in context of queueing theory

Recent interest:

Dynamics of gene expression under feedback
O Pulkkinen and J Berg. ArXiv: 0807.3521

Autocatalytic genetic networks modeled by piecewise-deterministic Markov processes
Zeiser S, Franz U, Liebscher V
J. Math. Biology 60: 207-246 (2010)

Non-equilibrium Thermodynamics of Piecewise Deterministic Markov Processes
Faggionato A, Gabrielli D, Crivellari MR
J. Stat. Phys. 137: 259-304 (2009)

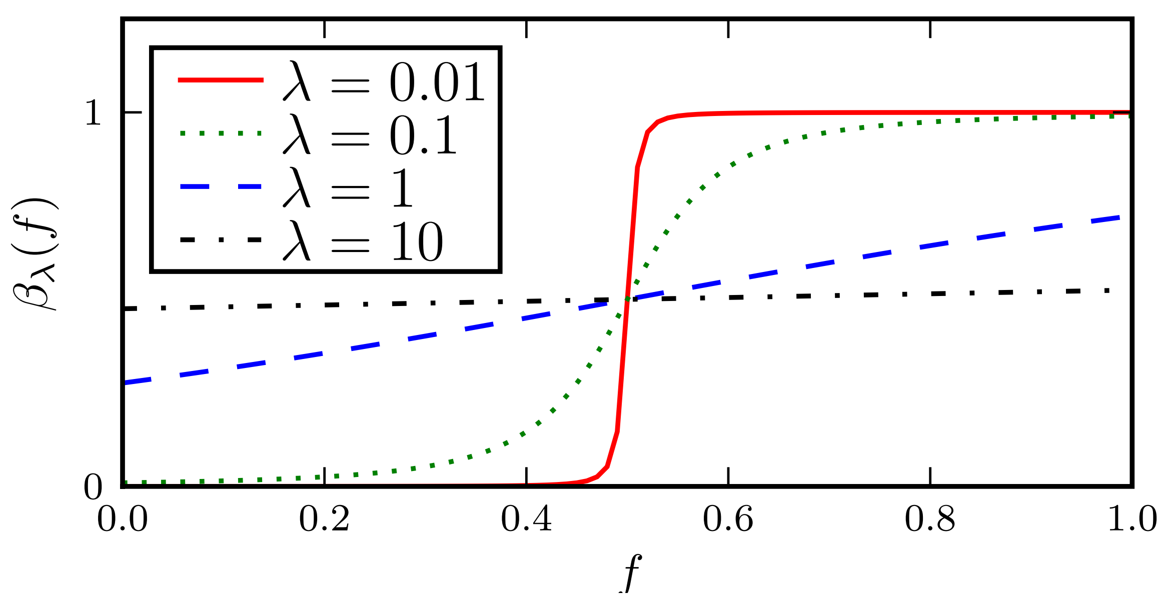
Characterisation of Catastrophes

Environmental response function (catastrophe rate)

$$\beta_\lambda(f) = \frac{1}{2}\left(1 + \frac{f - f^*}{\sqrt{\lambda^2 + (f - f^*)^2}}\right) .$$

limits $\lambda \gg 1 \rightarrow 1/2$ (Poisson process)

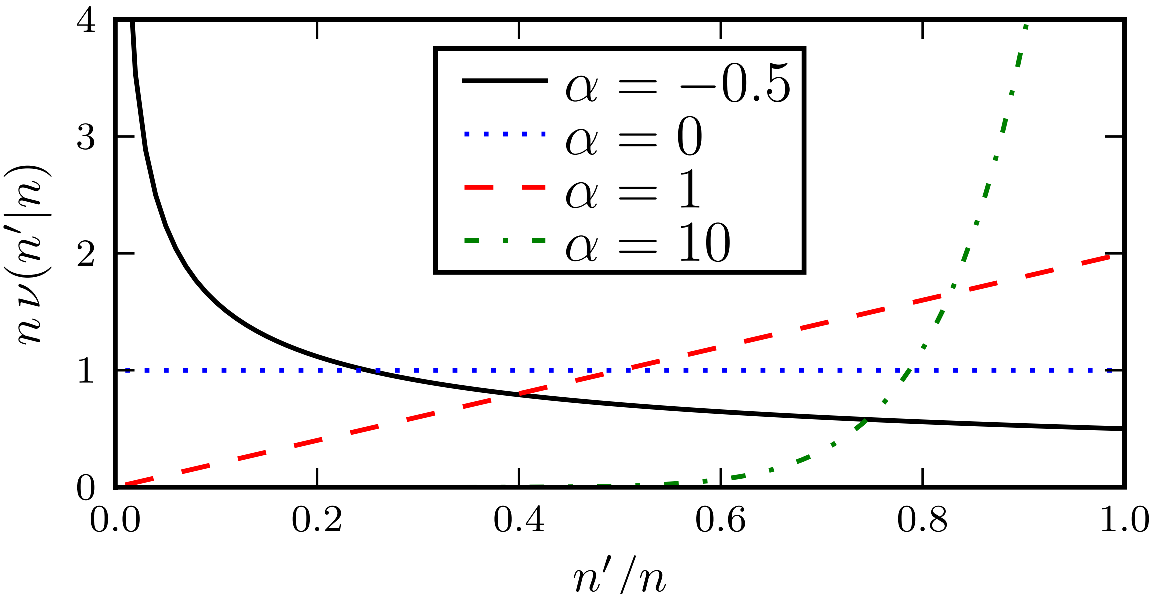
$\lambda \ll 1 \rightarrow \theta(f - f^*)$



Characterisation of Catastrophes

Take for catastrophe strength distribution

$$\nu(n'_A|n_A) = \theta(n_A - n'_A)\frac{(\alpha+1)}{n_A}\left(\frac{n'_A}{n_A}\right)^{\alpha} \quad \alpha > -1$$

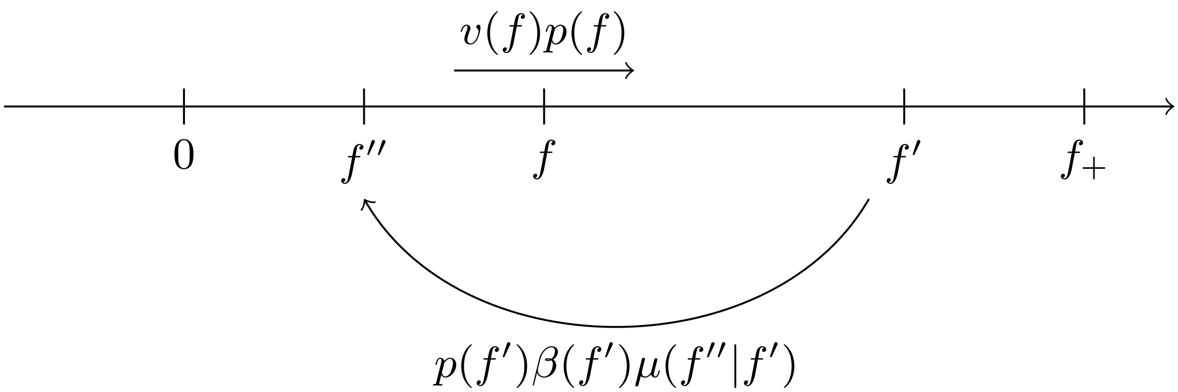


Then $f \to f' < f$ with distribution

$$\mu(f'|f) = \frac{1}{m(f)}\frac{\mathrm{d}m(f')}{\mathrm{d}f'} \quad m(f) = \left(\frac{f}{1-f}\right)^{1+\alpha}$$

Stationary distribution of $p(f)$

Probability flux balance:



$$v(f)p(f) = \int_f^{f_+} df' \int_0^f df'' \beta(f')p(f')\mu(f''|f')$$

Insert $\mu(f''|f') = \frac{1}{m(f')}\frac{\mathrm{d}m(f'')}{\mathrm{d}f''}$

$$\rightarrow \quad v(f)p(f) = \int_f^{f_+} \mathrm{d}f' \beta(f') P(f') \frac{m(f)}{m(f')}$$

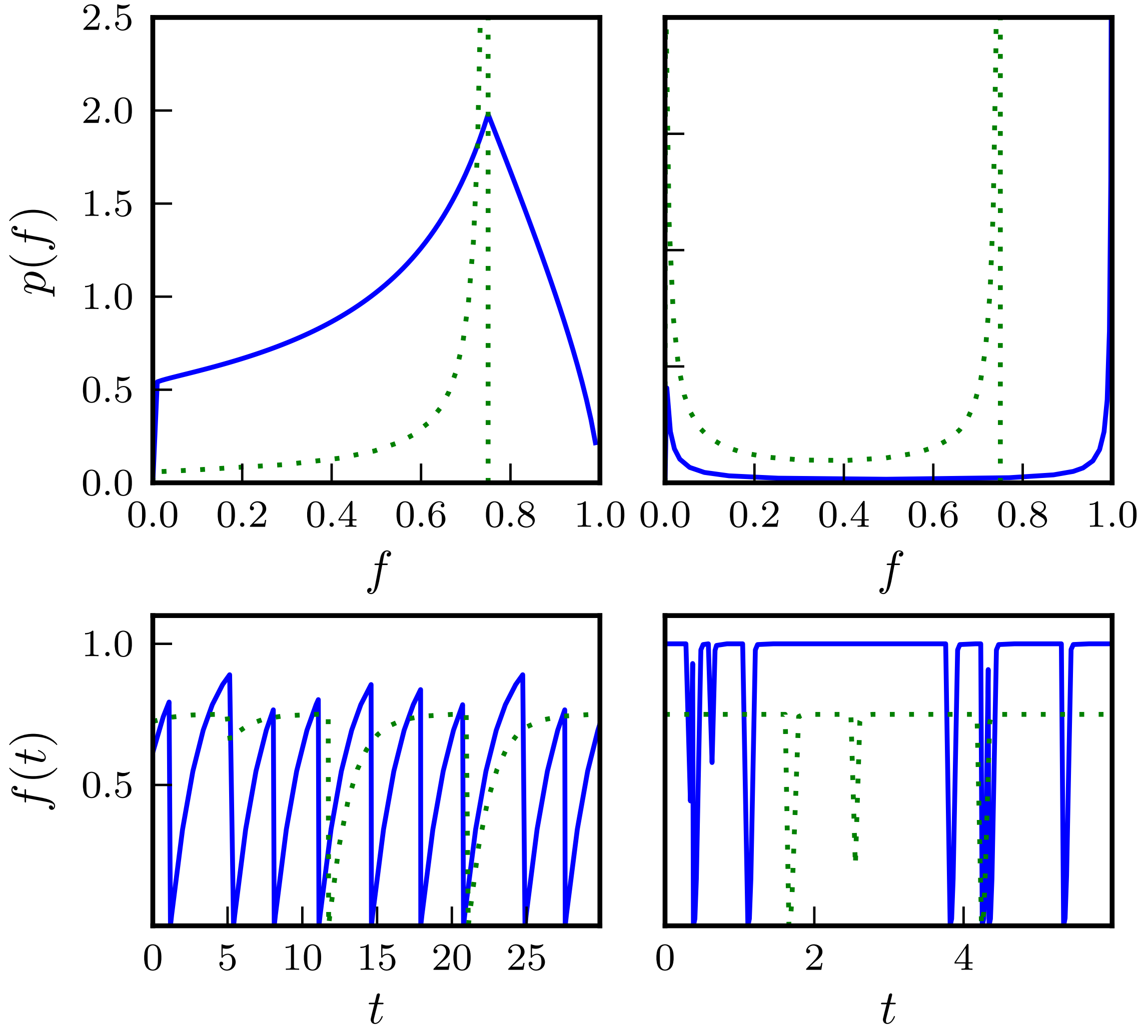
Solution

$$p(f) = C\frac{m(f)}{v(f)} \exp\left(-\int^f \mathrm{d}f' \ \frac{\beta(f')}{v(f')}\right)$$

Sample plots of $p(f)$ for $\lambda = 0$

Solid line: $k_A = 0$ $f_+ = 1$ $f_- = -k_B/\Delta\gamma$
Dashed line: k_A chosen so that $f_+ = f^*$

$\Delta\gamma = 0.1$ $\Delta\gamma = 100$

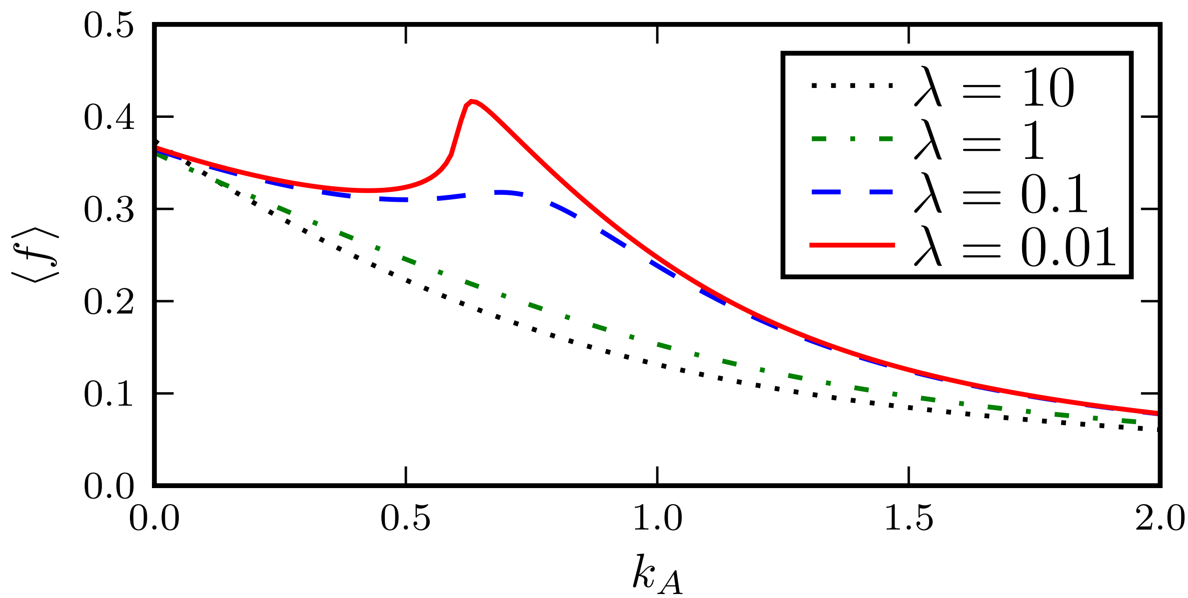


Optimal strategies

We characterise the population strategy by the value of k_A, which is the control parameter for the population balance.

We define **Optimal Strategies** as the values of k_A which maximise the average fitness $\langle f \rangle$ in the stationary state.

Two optimal strategies emerge:



Optimal strategies cont.

1. $k_A = 0$ (no switching to unfit state)
2. $k_A \simeq k_A^*$ where k_A^* yields $f_+ = f^*$ (Saturation fitness = threshold response)