Reading the Secrets of Biological Fluctuations

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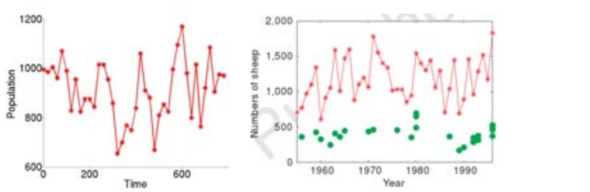
June 27, 2008

Why study fluctuations?

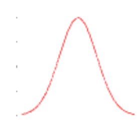
- Biology is noisy and we want to understand it.
- Stochasticity can drive phenomena we would miss in deterministic models.
- Fluctuations hold the key to deeper biological understanding?



Grenfell et al. (1998) *Nature*

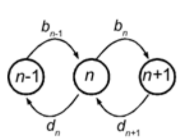
Variables at the Macroscopic and Individual Levels

- Deterministic models describe macroscopic behavior
- Individual based model are described by transition rates between states – a *Markov process*
- Macroscopic variable ϕ is independent of details of system (intensive), i.e. *population density*
- Individual-based variable n depends on system size (extensive), i.e. *population number*
- In a given area Ω with a macroscopic density ϕ, we'd expect to find $\langle n \rangle = \phi\Omega$ *on average*, which is more accurate with larger Ω.



Theory of Fluctuations

Markov process



$\Longrightarrow n = \Omega\phi + \Omega^{1/2}\xi \Longrightarrow$

Linear Noise Approximation

Fundamental Equations

$$\frac{\mathrm{d}\phi}{\mathrm{d}t} = \alpha_{1,0}(\phi) + \alpha''_{1,0}(\phi)\sigma^2 \qquad (1)$$

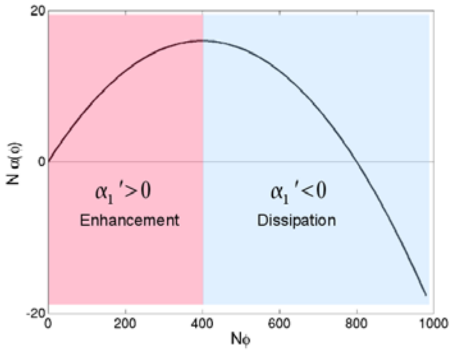
$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = 2\alpha'_{1,0}(\phi)\sigma^2 + \alpha_{2,0}(\phi) \qquad (2)$$

$$\alpha_{1,0}(\phi) = b(\phi) - d(\phi), \quad \alpha_{2,0} = b(\phi) + d(\phi)$$

Distinct Fluctuation Regimes

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \underbrace{c\frac{n}{N}\left(1-\frac{n}{N}\right)}_{b_n} - \underbrace{e\frac{n}{N}}_{d_n}$$

$$\frac{\mathrm{d}\sigma^2}{\mathrm{d}t} = 2\alpha_{1,0}'(\phi)\sigma^2 + \alpha_{2,0}(\phi)$$

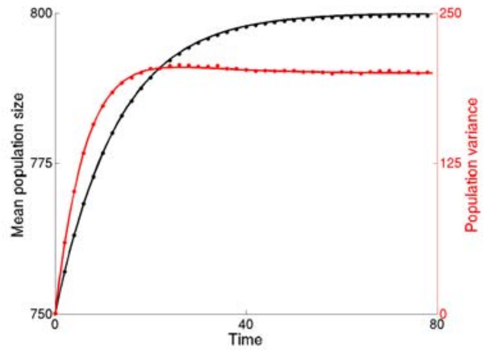


Near Equilibrium: Fluctuation Dissipation Regime

In the dissipation regime, fluctuations exponentially relax to the equilibrium level

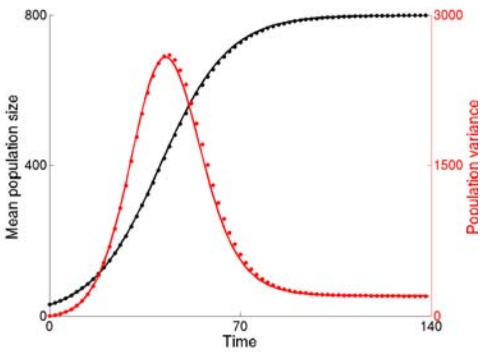
$$\hat{\sigma}^2 = \frac{b(n)+d(n)}{2[d'(n)-b'(n)]}$$

- $N = 1000$, $e = 0.2$, $c = 1$
- $\hat{n} = N\left[1-\frac{e}{c}\right] = 800$
- $\hat{\sigma}^2 = N\frac{e}{c} = 200$
- Dots are simulation averages, lines are theoretical prediction



Fluctuation Enhancement

With an initial condition starting deep in the enhancement regime, fluctuations grow exponentially. At $N = 400$, dissipation takes over and fluctuations return to the same equilibrium as before.

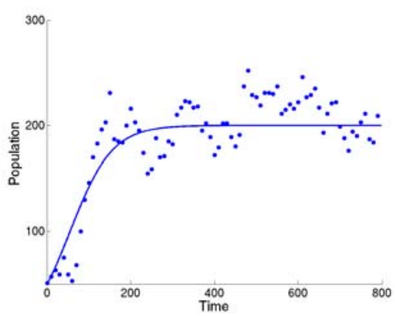


1. Noisy Biology
2. Fluctuation Regimes
3. **Model Choice**
4. Macroscopic Phenomena
5. Fluctuation Dominance

Which model best describes this data?

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \underbrace{c\frac{n}{N}\left(1-\frac{n}{N}\right)}_{b_n} - \underbrace{e\frac{n}{N}}_{d_n}$$

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \underbrace{rn}_{b_n} - \underbrace{\frac{rn^2}{K}}_{d_n}$$

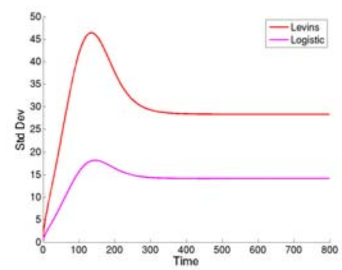


...and why does it matter?

Using the Information Hidden in the Fluctuations

1. Independently parameterize birth & death rates, see which is density dependent
2. Works with single realization at equilibrium
3. With replicates: The dynamic equations can determine functions $b(n)$ and $d(n)$
4. Uses more information to inform model choice
5. Can discount weights of points from high-variance regions when model-fitting

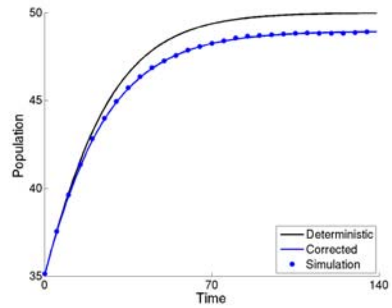
Predicted fluctuations



Stochastic Corrections: Deflation and Inflation

$$\frac{\mathrm{d}\phi}{\mathrm{d}t} = \alpha_{1,0}(\phi) + \alpha''_{1,0}(\phi)\sigma^2$$

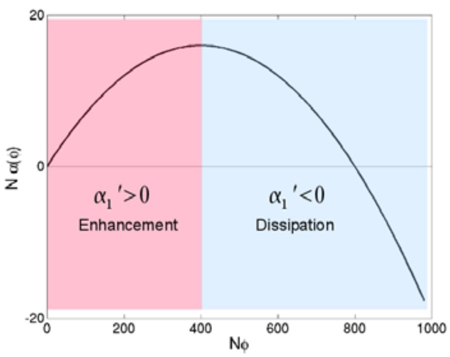
- $\alpha''_{1,0}(\phi) < 0 \implies$ Fluctuations suppress the average relative to the deterministic approximation.
- Our theory accurately predicts the extent of this effect.
- Recall $\alpha_{2,0} = b_n + d_n$ controls the magnitude of this effect.
- Ecological and evolutionary consequences for when variability is favorable?



Fluctuation Phenomena: Deflation

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \underbrace{c\frac{n}{N}\left(1-\frac{n}{N}\right)}_{b_n} - \underbrace{e\frac{n}{N}}_{d_n}$$

$$\frac{\mathrm{d}\phi}{\mathrm{d}t} = \alpha_{1,0}(\phi) + \alpha''_{1,0}(\phi)\sigma^2$$

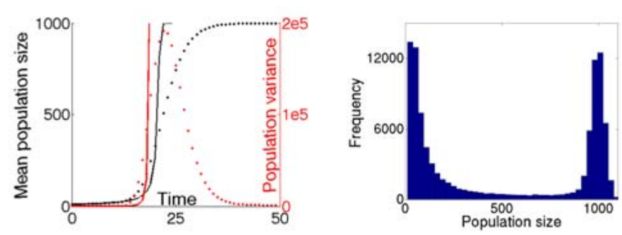


Fluctuation Dominance

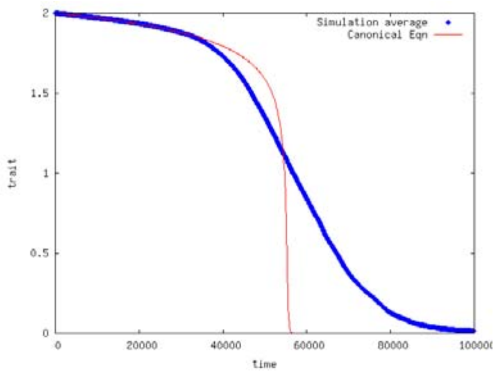
Far from equilibrium, enhancement can expand the fluctuations until they reach the macroscopic scale.

- Variance equation fails dramatically
- Mean trajectory need not follow the deterministic trajectory
- Bimodal distribution of trajectories can emerge
- **Conjecture:** occurs when neighborhood exists for which $\alpha_{1,0} \approx 0$ and $\alpha'_{1,0} \approx 0$

Breakdown of the approximation



Breakdown of the Canonical Equation of Adaptive Dynamics



Further Topics

This approach can be applied to a variety of stochastic processes in biology. . .

- **The multivariate theory**: multiple species or age structured populations. Predicts covariances as well.
- **Macroevolutionary theory**: inferring speciation and extinction rates from phylogenetic trees
- **Adaptive dynamics**: quantifying uncertainty in the canonical equation, correcting for fluctuations.

Acknowledgments

- Advisors & Advice
  - Alan Hastings
  - Joshua Weitz
  - Many here for helpful discussions!
- Funding
  - DOE CSGF
  - UC Davis Population Biology Graduate Group