Escaping from the boundary in Density Dependent Population Processes

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OUTLINE

DENSITY DEPENDENT MODELS: VERHULST'S LOGISTIC EQUATION

- One of the fundamental equations in ecology is Verhulst's logistic equation,

$$\dot{Y} = rY\left(1 - \frac{Y}{n}\right),$$

  which describes a self-limiting population.

- n is the "carrying capacity" of the population: net growth rates are negative when $X > n$.

- Replacing Y by $X = \frac{Y}{n}$, we arrive at a "nondimensionalized" version, with only one parameter r,

$$\dot{X} = rX(1 - X).$$

- Sometimes, we are most interested in population fluctuations, in which case we would like a stochastic model that approximates Verhulst's equation in some well-defined way.

DENSITY DEPENDENT MODELS: A STOCHASTIC LOGISTIC PROCESS

▶ A natural model is a continuous time Markov birth and death process, $Y(t)$, with rates

$$q_{Y,Y+1} = \beta Y \qquad q_{Y,Y-1} = \delta Y \left(1 + \gamma \frac{Y}{n}\right).$$

▶ Nondimensionalizing as before, we might consider instead the process $X^{(n)} = \frac{Y}{n}$, with rates

$$q^{(n)}_{X,X+\frac{1}{n}} = n\beta X \qquad q^{(n)}_{X,X-\frac{1}{n}} = n\delta X \left(1 + \gamma X\right).$$

▶ A quick calculation shows that

$$\mathbb{E}\left[\Delta X^{(n)}\right] = \mathbb{E}\left[\beta X^{(n)} - \delta X^{(n)}\left(1 + \gamma X^{(n)}\right)\right]\Delta t \quad \text{and} \quad \mathbb{E}\left[\left(\Delta X^{(n)}\right)^2\right] = \mathcal{O}\left(\tfrac{1}{n}\right),$$

suggesting that as n becomes large, $X^{(n)}$ should in some sense approach a limit X, satisfying a generalized logistic equation,

$$\dot{X} = \beta X - \delta X \left(1 + \gamma X\right).$$

DENSITY DEPENDENT POPULATION PROCESSES (KURTZ, 1970)

- In fact, we can make this convergence precise for a broad class of models, including the logistic process and many more of biological interest.
- Let $\{\lambda_{\mathbf{l}}^{(n)}(\mathbf{x})\}_{\mathbf{l}\in\mathbb{Z}^d}$ be a collection of non-negative functions defined on a subset $E \subseteq \mathbb{R}_+^d$. Set

$$E^{(n)} := E \cap \{n^{-1}\mathbf{k} : \mathbf{k} \in \mathbb{Z}^d\},$$

and assume that $\mathbf{x} \in E^{(n)}$ and $\lambda_{\mathbf{l}}^{(n)}(\mathbf{x}) > 0$ imply $\mathbf{x} + n^{-1}\mathbf{l} \in E^{(n)}$.

- The *density dependent family* corresponding to the $\lambda_{\mathbf{l}}^{(n)}(\mathbf{x})$ is a sequence $\{\mathbf{X}^{(n)}\}$ of jump Markov processes such that $\mathbf{X}^{(n)}$ has state space $E^{(n)}$ and intensities

$$q_{\mathbf{x},\mathbf{y}}^{(n)} = n\lambda_{n(\mathbf{y}-\mathbf{x})}^{(n)}(\mathbf{x}), \qquad \mathbf{x}, \mathbf{y} \in E^{(n)}.$$

DENSITY DEPENDENT POPULATION PROCESSES (KURTZ, 1970)

- Intuitively, we have a population consisting of a finite number of discrete individuals.
- Each individual has a type, which is indexed by an integer in the set $\{1, \ldots, d\}$; all individuals of a given type are identical.
- If $Y_i(t)$ is the number of individuals of type $i \in \{1, \ldots, d\}$ at time t, then $X_i^{(n)}(t)$ is the corresponding nondimensionalized process:

$$\mathbf{X}^{(n)}(t) = \left(X_1^{(n)}(t), \ldots, X_d^{(n)}(t) \right) = \frac{1}{n} \left(Y_1(t), \ldots, Y_d(t) \right).$$

- *e.g.*, Our logistic process corresponds to

$$\lambda_1^{(n)}(\mathbf{x}) = \beta x_1 \qquad \lambda_{-1}^{(n)}(\mathbf{x}) = \delta x_1 (1 - \gamma x_1).$$

THE "SYSTEM SIZE" n

- ▶ Much as in population genetics, we will be interested in obtaining limiting results as n tends to infinity.
- ▶ Unlike population genetics, n need not be a fixed population size, but rather an analogue of the carrying capacity in Verhulst's logistic equation.
- ▶ The number of individuals may vary stochastically, but, under the assumption of density dependence, after a transient phase, the total number of individuals will fluctuate about a value proportional to n.
- ▶ It can be interpreted differently in different models.
  - ▶ In a Gause-Lotka-Volterra model, it measures the size of the habitat, and thus the number of individuals it can sustain.
  - ▶ In an explicit resource model *e.g.,* of a chemostat, it might measure the volume of the reaction vessel.
  - ▶ In an epidemic models, it can be proportional to the number of uninfected hosts - the habitat for the pathogens.

EXAMPLE: A TWO STRAIN SIR MODEL WITH DEMOGRAPHY
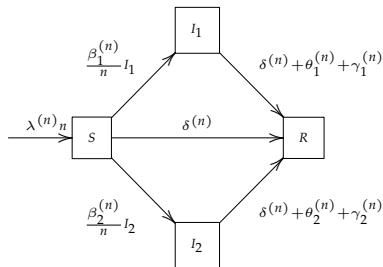
Parameter	Description
$\kappa^{(n)} n$	birth/immigration rate for susceptibles
$\delta^{(n)}$	base mortality rate
$\beta_i^{(n)}$	contact rate for disease i
$\theta_i^{(n)}$	excess mortality for disease i
$\gamma_i^{(n)}$	recovery rate for disease i
$\alpha_i^{(n)}$	$\alpha_i^{(n)} = \theta_i^{(n)} + \gamma_i^{(n)}$

- Population is grouped into *susceptibles*, $S(t)$, *infectives*, $I_i(t)$, and *removed* individuals, $R(t)$.
- Assume cross-immunity between strains, no coinfection.
- The "system-size" n is proportional to the *average* host population size. The actual number of individuals fluctuates stochastically.

DENSITY DEPENDENT POPULATION PROCESS FORMULATION

- Model is completely described by $(S(t), I_1(t), I_2(t))$ – can ignore removed individuals.
- Get a continuous-time Markov process taking values in $\mathbb{N}_0^3$ with rates

$$\mathbb{P}\{S(t + \Delta t) = S(t) + 1\} = \kappa^{(n)} n \Delta t + o(\Delta t)$$

$$\mathbb{P}\{S(t + \Delta t) = S(t) - 1\} = \delta^{(n)} S(t) \Delta t + o(\Delta t)$$

$$\mathbb{P}\{(S(t + \Delta t), I_i(t + \Delta t)) = (S(t) - 1, I_i(t) + 1)\} = \frac{\beta_i^{(n)} S I_i(t)}{n} \Delta t + o(\Delta t)$$

$$\mathbb{P}\{I_i(t + \Delta t) = I_i(t) - 1\} = (\delta^{(n)} + \alpha_i^{(n)}) I_i \Delta t + o(\Delta t)$$

- $(X^{(n)}(t), Y_1^{(n)}(t), Y_2^{(n)}(t)) = \frac{1}{n}(S(t), I_1(t), I_2(t))$ is a density dependent family with rates

$$\lambda_{\mathbf{e}_1}^{(n)}(x, y_1, y_2) = \kappa^{(n)} \quad \lambda_{-\mathbf{e}_1}^{(n)}(x, y_1, y_2) = \delta^{(n)} x$$

$$\lambda_{-\mathbf{e}_1 + \mathbf{e}_2}^{(n)}(x, y_1, y_2) = \beta_1^{(n)} x y_1 \quad \lambda_{-\mathbf{e}_2}^{(n)}(x, y_1, y_2) = (\delta^{(n)} + \alpha_1^{(n)}) y_1$$

$$\lambda_{-\mathbf{e}_1 + \mathbf{e}_3}^{(n)}(x, y_1, y_2) = \beta_2^{(n)} x y_2 \quad \lambda_{-\mathbf{e}_3}^{(n)}(x, y_1, y_2) = (\delta^{(n)} + \alpha_2^{(n)}) y_2.$$

LAW OF LARGE NUMBERS (KURTZ, 1970)

- Let $\{\lambda_l^{(n)}(\mathbf{x})\}_{l\in\mathbb{Z}^d}$ be as above and let $\{\mathbf{X}^{(n)}\}$ be the corresponding density-dependent family.
- Assume that there exist functions $\{\lambda_l(\mathbf{x})\}_{l\in\mathbb{Z}^d}$ such that

$$\lim_{n\to\infty} \sum_{l\in\mathbb{Z}^K} \|l\| \sup_{\mathbf{x}\in\mathcal{K}} \left|\lambda_l^{(n)}(\mathbf{x}) - \lambda_l(\mathbf{x})\right| = 0 \quad \text{and} \quad \sum_{l\in\mathbb{Z}^d} \|l\| \sup_{\mathbf{x}\in\mathcal{K}} \lambda_l(\mathbf{x}) < \infty$$

  for all compact sets $\mathcal{K} \subset E$.
- Let $\mathbf{F}(\mathbf{x}) = \sum_{l\in\mathbb{Z}^d} l\lambda_l(\mathbf{x})$, and suppose $\mathbf{F}$ is locally Lipschitz.
- Suppose $\mathbf{X}^{(n)}(0) \to \mathbf{x}_0$ and let $\mathbf{X}(t, \mathbf{x}_0)$ satisfy

$$\dot{\mathbf{X}} = \mathbf{F}(\mathbf{X}).$$

  with $\mathbf{X}(0, \mathbf{x}_0) = \mathbf{x}_0$
- Then, for any fixed $T > 0$,

$$\lim_{n\to\infty} \sup_{t \leq T} \left|\mathbf{X}^{(n)}(t) - \mathbf{X}(t, \mathbf{x}_0)\right| = 0 \quad \text{a.s.}$$

LAW OF LARGE NUMBERS: EXAMPLES

▸ As we might hope, for the stochastic logistic model, the limiting deterministic process is

$$\dot{X} = \beta X - \delta X \left(1 + \gamma X\right).$$

▸ For the two strain SIR model with demography, if we assume that $\lambda^n = \lambda + \mathcal{O}\left(\frac{1}{n}\right)$, $\delta^n = \delta + \mathcal{O}\left(\frac{1}{n}\right)$, *etc.* Then the law of large numbers limit $(X(t), Y_1(t), Y_2(t))$ satisfies the standard ODE for multi-strain SIR:

$$
\begin{aligned}
\dot{X}(t) &= \kappa - \left(\beta_1 Y_1(t) + \beta_2 Y_2(t) + \delta\right) X(t) \\
\dot{Y}_i(t) &= \left(\beta_i X(t) - (\delta + \alpha_i)\right) Y_i(t)
\end{aligned}
$$

CENTRAL LIMIT THEOREM (KURTZ, 1971)

- Assume in addition that

$$\lim_{n\to\infty} \sqrt{n} \sum_{\mathbf{l}\in\mathbb{Z}^K} \|\mathbf{l}\| \sup_{\mathbf{x}\in\mathcal{K}} \left|\lambda_\mathbf{l}^{(n)}(\mathbf{x}) - \lambda_\mathbf{l}(\mathbf{x})\right| = 0 \quad \text{and} \quad \sum_{\mathbf{l}\in\mathbb{Z}^d} \|\mathbf{l}\|^2 \sup_{\mathbf{x}\in\mathcal{K}} \lambda_\mathbf{l}(\mathbf{x}) < \infty.$$

- Let $\mathbf{V}^{(n)} = \sqrt{n}(\mathbf{X}^{(n)} - \mathbf{X})$ and suppose that $V^{(n)}(0) \to V(0)$.

- Then, $\mathbf{V}^{(n)} \Rightarrow \mathbf{V}$ in $\mathbb{D}_E[0,\infty)$, where $\mathbf{V}$ satisfies

$$\mathbf{V}(t) = \mathbf{V}(0) + \int_0^t \mathbf{DF}(\mathbf{X}(s,\mathbf{x}_0))\mathbf{V}(s)\,ds + \sum_{\mathbf{l}\in\mathbb{Z}^d} \mathbf{l} \int_0^t \sqrt{\lambda_\mathbf{l}(\mathbf{X}(s),\mathbf{x}_0)}\,dB_\mathbf{l}(s)$$

and the $B_\mathbf{l}$ are independent standard Brownian motions.

LARGE DEVIATIONS PRINCIPLE (WENTZELL, 1976)

- Let

$$H(\mathbf{x}, \boldsymbol{\alpha}) = \sum_{\mathbf{l} \in \mathbb{Z}^d} (e^{\boldsymbol{\alpha} \cdot \mathbf{l}} - 1) \lambda_{\mathbf{l}}(\mathbf{x}),$$

$$L(\mathbf{x}, \boldsymbol{\beta}) = \sup_{\boldsymbol{\alpha} \in E} \boldsymbol{\alpha} \cdot \boldsymbol{\beta} - H(\mathbf{x}, \boldsymbol{\alpha}),$$

and, for $\varphi(t) \in C_E[0, T]$ satisfying $\varphi(0) = \mathbf{x}_0$, set

$$I_{\mathbf{x}_0, T}(\varphi) = \int_0^T L(\varphi(t), \dot{\varphi}(t)) \, dt$$

- Provided

$$\sup_{\mathbf{x} \in \mathbb{R}^n} H(\mathbf{x}, \boldsymbol{\alpha}) < \infty,$$

and

$$\lim_{\eta \to 0} \sup_{\|\mathbf{x} - \mathbf{y}\| < \eta} \frac{L(\mathbf{y}, \boldsymbol{\beta}) - L(\mathbf{x}, \boldsymbol{\beta})}{1 + L(\mathbf{x}, \boldsymbol{\beta})} = 0$$

for all $\boldsymbol{\alpha}, \boldsymbol{\beta} \in \mathbb{R}^d$, then $I_{\mathbf{x}, T}(\varphi)$ is a good rate function for the family $\mathbf{X}^{(n)}$.

OUTLINE

ESCAPING FROM THE BOUNDARY

- All of the previous explicitly or implicitly assumed that there exists $\varepsilon > 0$ such that $X_i^{(n)}(t) > \varepsilon$ *i.e.*, the absolute number of individuals is greater than εn.
- Once this is true, the process is essentially deterministic, with an exponentially small probability of moving macroscopically away from the trajectories of a deterministic process.
- However, in many problems of evolutionary interest, we are most concerned about the stochastic process starting from a single individual.
- The primary question then becomes whether that individual can produce sufficiently many offspring to pass into the deterministic regime *i.e.*, escape the boundary.
- As we've already seen several times since yesterday, we can approach this problem via branching processes. My question (which I won't answer completely today) is to ask how generally we can apply this approach.

DENSITY DEPENDENT BIRTH-DEATH PROCESSES

▶ For escape from the boundary to be an interesting question, we need an absorbing boundary. For simplicity, assume that $\{\mathbf{x} : x_1 = 0\}$ is the boundary of interest, and that

$$\lambda_{\mathbf{l}}^{(n)}(\mathbf{x}) = \begin{cases} \beta_{1,l}^{(n)}(\mathbf{x})x_1 & \text{if } \mathbf{l} = l\mathbf{e}_1 \\ \delta_1^{(n)}(\mathbf{x})x_1 & \text{if } \mathbf{l} = -\mathbf{e}_1 \\ 0 & \text{for all other } \mathbf{l} \text{ with } l_1 \neq 0 \end{cases}$$

▶ Thus, $F_1(\mathbf{x}) = f_1(\mathbf{x})x_1$ for

$$f_1(\mathbf{x}) = \sum_{l=1}^{\infty} l\beta_{1,l}(\mathbf{x}) - \delta_1^{(n)}(\mathbf{x})$$

and $\{\mathbf{x} : x_1 = 0\}$ is invariant for the law of large numbers dynamical system.

▶ I will further assume that there exists a compact set $\mathcal{K}$ that contains a neighbourhood of the origin and is invariant under the flows of $\mathbf{F}(\mathbf{x})$.

"BRANCHING PROCESS APPROXIMATION"

- ► Let $\mathbf{x}_0 \in \{\mathbf{x} : x_1 = 0\}$ and let $\mathbf{X}(t, \mathbf{x}_0)$ be the corresponding law of large numbers trajectory.
- ► By our previous assumption, $\mathbf{X}(t, \mathbf{x}_0) \in \{\mathbf{x} : x_1 = 0\}$ for all $t > 0$.
- ► Let $Z(t)$ be the time-inhomogeneous branching process with rates

$$\beta_{i,l}(\mathbf{X}(t, \mathbf{x}_0)) \quad \text{and} \quad \delta_i(\mathbf{X}(t, \mathbf{x}_0)),$$

i.e., $Z(t)$ is obtained by replacing the full stochastic process $\mathbf{X}^{(n)}(t)$ by it's deterministic approximation in the definition of $X_1^{(n)}(t)$.

- ► Morally, $Z(t)$ is the "branching process approximation", but to justify that, we need to do some more work.
- ► First, let's look at some properties of $Z(t)$

THE BRANCHING PROCESS $Z(t)$

- ► Let $\bar{\beta}(\mathbf{x}) = \sum_{l=1}^{\infty} l\beta_{1,l}(\mathbf{x})$ and $\hat{\beta}(\mathbf{x}) = \sum_{l=1}^{\infty} l^2\beta_{1,l}(\mathbf{x})$
- ► $Z(t)$ has mean $m(t) = \mathbb{E}[X_i(t)] = e^{\int_0^t \bar{\beta}_1(\mathbf{X}(u,\mathbf{x}_0)) - \delta_1(\mathbf{X}(u,\mathbf{x}_0))\, du}$ and variance
  $\mathrm{Var}(Z(t)) = \int_0^t e^{2\int_s^t \bar{\beta}(\mathbf{X}(u,\mathbf{x}_0)) - \delta(\mathbf{X}(u,\mathbf{x}_0))\, du} \left(\hat{\beta}(\mathbf{X}(s,\mathbf{x}_0)) + \delta(\mathbf{X}(s,\mathbf{x}_0)) \right)\, ds.$
- ► $\hat{\beta}(\mathbf{x}) \geq \bar{\beta}(\mathbf{x})$, with equality if and only if $\beta_{1,l}(\mathbf{x}) \equiv 0$ for $l > 1$.
- ► Let $q(\mathbf{x}_0, t) = \mathbb{P}\{X_1(t) = 0\}$

$$\frac{\int_0^t e^{-\int_0^s \bar{\beta}_1(\mathbf{X}(u,\mathbf{x}_0)) - \delta_1(\mathbf{X}(u,\mathbf{x}_0))\, du} \delta_1(\mathbf{X}(s,\mathbf{x}_0))\, ds}{1 + \int_0^t e^{-\int_0^s \bar{\beta}_1(\mathbf{X}(u,\mathbf{x}_0)) - \delta_1(\mathbf{X}(u,\mathbf{x}_0))\, du} \delta_1(\mathbf{X}(s,\mathbf{x}_0))\, ds} \leq q(\mathbf{x}_0, t)$$

$$\leq \frac{\int_0^t e^{-\int_0^s \bar{\beta}_1(\mathbf{X}(u,\mathbf{x}_0)) - \delta_1(\mathbf{X}(u,\mathbf{x}_0))\, du} \left(\delta_1(\mathbf{X}(s,\mathbf{x}_0)) + \frac{\bar{\beta}_1(\mathbf{X}(s,\mathbf{x}_0)) - \hat{\beta}(\mathbf{X}(s,\mathbf{x}_0))}{2} \right)\, ds}{1 + \int_0^t e^{-\int_0^s \bar{\beta}_1(\mathbf{X}(u,\mathbf{x}_0)) - \delta_1(\mathbf{X}(u,\mathbf{x}_0))\, du} \left(\delta_1(\mathbf{X}(s,\mathbf{x}_0)) + \frac{\bar{\beta}_1(\mathbf{X}(s,\mathbf{x}_0)) - \hat{\beta}(\mathbf{X}(s,\mathbf{x}_0))}{2} \right)\, ds},$$

- ► Thus,

$$\int_0^t e^{-\int_0^s \bar{\beta}_1(\mathbf{X}(u,\mathbf{x}_0)) - \delta_1(\mathbf{X}(u,\mathbf{x}_0))\, du} \delta_1(\mathbf{X}(s,\mathbf{x}_0))\, ds < \infty$$

- ► The convergence of the integrals on the left and right, say I_- and I_+ give
  necessary and sufficient conditions, respectively, for the process to have
  a non-zero probability of persisting indefinitely, but unfortunately,
  neither is necessary and sufficient.

SUPERCRITICAL PROCESSES

- ► Assume $I_-, I_+ < \infty$.
- ► Then, $W(t) = \frac{Z(t)}{m(t)}$ is a martingale with $\mathbb{E}\left[W(t)\right] = 1$ and

$$W := \lim_{t \to \infty} W(t)$$

  exists pointwise almost surely.

- ► Provided

$$\mathbb{E}\left[W(t)^2 \Big| Z(s) = 1\right] = 1 + \int_s^t e^{-2\int_0^\tau \bar{\beta}(u) - \delta(u)\, du}\left(\hat{\beta}(\tau) + \delta(\tau)\right)\, d\tau,$$

  is bounded for all s, t, $W(t) \to W$ in $L^2(\mathbb{P})$ as well abd $\mathbb{E}\left[W\right] = 1$.

- ► If we assume that

$$\inf_{s \geq 0} \int_s^\infty e^{-\int_s^\tau \sum_{n=1}^\infty \beta_n(u) + \delta(u)\, du}\delta(\tau)\, d\tau > p > 0$$

  i.e., the probability of an individual dying without offspring is bounded below, then

$$q(\infty, \mathbf{x}_0) := \lim_{t \to \infty} q(t, \mathbf{x}_0) = \mathbb{P}\left\{W = 0\right\}.$$

LYAPUNOV EXPONENTS AND MALTHUSIAN PARAMETERS

- Let $\chi_1(\mathbf{x}_0) = \lim_{t \to \infty} \frac{1}{t} \int_0^t f_1(\mathbf{X}(u, \mathbf{x}_0))\, du$.
- $\chi_1(\mathbf{x}_0)$ is also a boundary Lyapunov exponent for the dynamical system.
- If $\mathbf{x}_0$ is in the basin of a stable attractor $\mathbf{x}^\star$, then $\chi_1(\mathbf{x}_0) = f_1(\mathbf{x}^\star)$.
- If $\omega(\mathbf{x}_0)$ is a stable limit cycle of period T, say $\gamma(t)$, then
  $\chi_1(\mathbf{x}_0) = \frac{1}{T} \int_0^T f_d(\gamma(u))\, du$.
- By Birkhoff's ergodic theorem, $\chi_1(\mathbf{x}_0) = \int f_d(\mathbf{x})\mu(d\mathbf{x})$ for μ-almost all $\mathbf{x}$, for some ergodic measure μ.
- If $\chi_1(\mathbf{x}_0) > 0$, then $I_+ < \infty$ and the probability of reaching εN is > 0.
- If $\chi_1(\mathbf{x}_0) < 0$, then $I_- = \infty$ and the probability of reaching εN is 0.
- If $I_+ < \infty$, then $\chi_1(\mathbf{x}_0) \geq 0$.
- If $I_- = \infty$, then $\chi_1(\mathbf{x}_0) \leq 0$.
- Cases when $\chi_1(\mathbf{x}_0) = 0$ are more subtle; partial results available.
- Thus, $\chi_1(\mathbf{x}_0)$ is analogous to the Mathusian parameter for a homogeneous branching process.

MALTHUSIAN PARAMETERS AND HITTING TIMES

- ▶ If the limit converges sufficiently fast (*e.g.*, in the cases of a stable fixed point or stable limit cycle, convergence is exponentially fast)

$$\phi = \lim_{t \to \infty} e^{-\chi_1(\mathbf{x}_0)t} m(t)$$

exists and is finite.

- ▶ If in addition, $\chi_1(\mathbf{x}_0) > 0$, then

$$\lim_{t \to \infty} e^{-\chi_1(\mathbf{x}_0)t} Z(t) = W \quad \text{a.s.}$$

and in L^2.

- ▶ In particular, if $M > 0$ and $\tau_M = \inf\{t : Z(t) \geq M\}$, then

$$\tau_M - \frac{1}{\chi_1(\mathbf{x}_0)} \ln M \to -\frac{1}{\chi_1(\mathbf{x}_0)} (\ln W + \ln \phi).$$

so that $\frac{\mathbb{E}_1[\tau_M]}{\ln M} \to \frac{1}{\chi_1(\mathbf{x}_0)}$.

- ▶ One can also show that if $\chi_1(\mathbf{x}_0) < 0$ and $\tau_0 = \inf\{t : Z(t) = 0\}$, then $\frac{\mathbb{E}_M[\tau_0]}{\ln M} \to \frac{1}{|\chi_1(\mathbf{x}_0)|}$.

OUTLINE

TRAPPING BRANCHING PROCESSES

Fix $\mathbf{X}(0) = \mathbf{x}_0 \in \{\mathbf{x} : x_1 = 0\} \cap \mathcal{K}$ and fix $\varepsilon > 0$ sufficiently small that

$$\mathcal{K}_{\mathbf{x}_0,\varepsilon}(t) = \overline{\{\mathbf{x} \in \mathbb{R}_+^d : \|\mathbf{x} - X(t)\| < \varepsilon\}} \quad \text{and} \quad \mathcal{K}_{\mathbf{x}_0,\varepsilon} = \cup_{t \geq 0} \mathcal{K}_{\mathbf{x}_0,\varepsilon}(t)$$

are contained in $\mathcal{K}$.

Under the assumptions of the law of large numbers, there exists n_ε such that

$$\sum_l l \sup_{\mathbf{x} \in \mathcal{K}} \left| \beta_{1,l}^{(n)}(\mathbf{x}) - \beta_{1,l}(\mathbf{x}) \right| + \left| \delta_1^{(n)}(\mathbf{x}) - \delta_1(\mathbf{x}) \right| < \varepsilon$$

for $n \geq n_\varepsilon$. Set

$$\epsilon_l(\mathcal{K}) = \begin{cases} \sup_{\mathbf{x} \in \mathcal{K}} \left| \beta_{1,l}^{(n_\varepsilon)}(\mathbf{x}) - \beta_{1,l}(\mathbf{x}) \right| & \text{if } l > 1 \\ \sup_{\mathbf{x} \in \mathcal{K}} \left| \delta_1^{(n)}(\mathbf{x}) - \delta_1(\mathbf{x}) \right| & \text{if } l = -1 \end{cases}$$

and let

$$\beta_{1,l}^{+\varepsilon}(t) = \sup_{\mathbf{x} \in \mathcal{K}_{\mathbf{x}_0,\varepsilon}(t)} \beta_{1,l}(\mathbf{x}) + \epsilon_l(\mathcal{K}), \quad \beta_{1,l}^{-\varepsilon}(t) = \inf_{\mathbf{x} \in \mathcal{K}_{\mathbf{x}_0,\varepsilon}(t)} \beta_{1,l}(\mathbf{x}) - \epsilon_l(\mathcal{K}),$$

$$\delta_1^{+\varepsilon}(t) = \sup_{\mathbf{x} \in \mathcal{K}_{\mathbf{x}_0,\varepsilon}(t)} \delta_1(\mathbf{x}) + \epsilon_{-1}(\mathcal{K}), \quad \text{and} \quad \delta_1^{-\varepsilon}(t) = \inf_{\mathbf{x} \in \mathcal{K}_{\mathbf{x}_0,\varepsilon}(t)} \delta_1(\mathbf{x}) - \epsilon_{-1}(\mathcal{K}).$$

Under the assumptions of the central limit theorem, we can take $\varepsilon = \varepsilon_n$ provided $\liminf_{n \to \infty} \sqrt{n} \varepsilon_n > 0$.

COUPLING

- Let $\tau_{i,\varepsilon,n} = \inf\{t : X_i^{(n)}(t) \geq \varepsilon n\}$.
- If the remaining Lyapunov exponents are negative, under suitable conditions (Lyapunov-Perron regularity), with high probability, one can construct coupled branching processes $Z(t)$ (as previously), $Z^{-\varepsilon}(t)$ with rates

$$\beta_{i,l}^{-\varepsilon}(t) \quad \text{and} \quad \delta_i^{+\varepsilon}(t)$$

  and $Z^{+\varepsilon}(t)$ with rates

$$\beta_{1,l}^{+\varepsilon}(t) \quad \text{and} \quad \delta_1^{-\varepsilon}(t),$$

  such that

$$Z^{-\varepsilon}(t) \leq Z(t) \leq Z^{+\varepsilon}(t)$$

  and

$$Z^{-\varepsilon}(t) \leq X_i^{(n)}(t) \leq Z^{+\varepsilon}(t)$$

  for all $t < \tau_{1,\varepsilon,n}$ and n sufficiently large.
- The coupling holds provided $\tau_{i,\varepsilon,n} > \tau_{1,\varepsilon,n}$ for all $i > 1$; the Lyapunov conditions ensure this happens with high probability.

TWO-STAGE COUPLING

In practice, one needs to consider two "layers" of coupling. For the first layer, we can choose sequences ε_n and $t_n \propto \ln n$ so that

- $\varepsilon_n \to 0$ and $\sqrt{n}\varepsilon_n \to \infty$.
- If $X_1^{(n)}(t_n) > 0$, then $\sqrt{n} \ll X_1^{(n)}(t_n) \ll \varepsilon_n n$, and
- $\dfrac{Z^{\pm \varepsilon_n}(t_n)}{\mathbb{E}\left[Z^{\pm \varepsilon_n}, (t_n)\right]} \to W$, and thus $\dfrac{X_1^{(n)}(t_n)}{\mathbb{E}\left[X_1^{(n)}(t_n)\right]} \to W$

Once $X_1^{(n)}(t_n) \gg \sqrt{n}$, nonlinear terms can prevent us from "squeezing" the couplings together.

- Fix $\varepsilon > 0$ and let $Z_j^{\pm \varepsilon}$ be i.i.d. copies of $Z^{\pm \varepsilon}$ started from one individual:

$$\sum_{j=1}^{X_1^{(n)}(t_n)} Z_j^{-\varepsilon}(t) \leq X_1^{(n)}(t + t_n) \leq \sum_{j=1}^{X_1^{(n)}(t_n)} Z_j^{+\varepsilon}(t).$$

- Let $q_{\varepsilon, \pm}$ be extinction probabilities for $Z^{\pm \varepsilon}$. Then,

$$q_{\varepsilon, +}^{X_1^{(n)}(t_n)} \leq \mathbb{P}\left(\tau_{1, \varepsilon, n} = +\infty\right) \leq q_{\varepsilon, -}^{X_1^{(n)}(t_n)},$$

so, if $X_1^{(n)}(t_n) > 0$, $\mathbb{P}\left(\tau_{1, \varepsilon, n} = +\infty\right) \to 1$ as $n \to \infty$.

CONSEQUENCES

- $\lim_{n \to \infty} \mathbb{P}\left\{X_1^{(n)}(t) = 0\right\} = q(\mathbf{x}_0, t) = \mathbb{P}\{Z(t) = 0\}$ and
  $\lim_{n \to \infty} \mathbb{P}\left\{X_i^{(n)}(t) > \varepsilon n\right\} = 1 - q(\mathbf{x}_0, +\infty)$.

- Thus, the values escape probabilities are independent of ε (though, to be clear the proof requires a suitable choice of ε.

- The law of large numbers also tells us that

$$\frac{X_1^{(n)}(t + t_n)}{X_1^{(n)}(t_n)} \to e^{\int_0^t f_1(\mathbf{X}(u, \mathbf{x}_0)\, du},$$

i.e., that the trajectories are essentially deterministic and follow the deterministic trajectories once the population has reached $\varepsilon_n n$ individuals. One can use expressions for $\tau_{1, \varepsilon, n}$ to obtain more detailed estimates when the trajectory approaches a fixed point $\mathbf{x}^\star$.

- One can also proceed similarly with estimates of the extinction time to obtain the time for a selective sweep, *e.g.,* for an invader 1 replacing a resident 2, and a sweep from a saddle $\mathbf{x}_0$ to a fixed point $\mathbf{x}^\star$, one has

$$\frac{\mathbb{E}_1[\tau_{1, \varepsilon, n}]}{\ln n} \to \frac{1}{\chi_1(\mathbf{x}_0)} + \frac{1}{\chi_2(\mathbf{x}^\star)}.$$

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TWO STRAIN SIR MODEL

Consider a single individual infected with strain 2 entering a population where strain 1 is endemic. Then, as $n \to \infty$, the probability strain 2 dies out is

$$q = \frac{\int_0^\infty e^{-\int_0^s \beta_2 X(u) - (\delta + \alpha_2)) \, du}(\delta + \alpha_2)) \, ds}{1 + \int_0^\infty e^{-\int_0^s \beta_2 X(u) - (\delta + \alpha_2)) \, du}(\delta + \alpha_2)) \, ds},$$
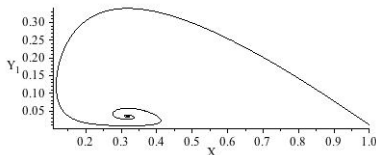
where $X(t)$ and $Y_1(t)$ satisfy

$$\begin{array}{rcl}
\dot{X}(t) & = & \lambda - (\beta_1 Y_1(t) + \delta) \, X(t) \\
\dot{Y}_1(t) & = & (\beta_1 X(t) - (\delta + \alpha_1)) \, Y_1(t)
\end{array}$$

with $X(0) = x$ and $Y_1(0) = y_1$. The probability strain 2 fixes is asymptotic to $1 - q$.

SIR NEAR EQUILIBRIUM

► The ith *basic reproduction number* is $\mathfrak{R}_{0,i} = \frac{\beta_i}{\delta + \alpha_i}$

► As $t \to \infty$, $(X(t), Y_1(t))$ tend to equilibrium $\left(\frac{1}{\mathfrak{R}_{0,1}}, \frac{1}{\beta_1} \left(\frac{\lambda}{\mathfrak{R}_{0,1}} - \delta \right) \right)$.

Parameter values: $\lambda = \delta = \frac{1}{60}$, $\mathfrak{R}_{0,1} = 3$, $\alpha_1 = \frac{1}{3}$.

► If we assume that strain 2 arrives at $t = 0$ and strain 1 is at this endemic equilibrium, $X(t) = \frac{1}{\mathfrak{R}_{0,1}}$ for all t, the probability that strain 2 eventually fixes is

$$1 - q = \begin{cases} 1 - \frac{\mathfrak{R}_{0,1}}{\mathfrak{R}_{0,2}} & \text{if } \mathfrak{R}_{0,2} > \mathfrak{R}_{0,1}, \\ 0 & \text{otherwise.} \end{cases}$$

► Conforms with the idea that the R_0's tell the whole story.

FIXATION PROBABILITY: PERTURBATION

- We've assumed that strain 2 arises after strain 1 is at equilibrium, but we don't need to do this.
- Consider a perturbation and linearize $(X(t), Y_1(t))$ about equilibrium:

$$X(t) = \frac{1}{\mathfrak{R}_{0,1}} + \xi(t) \qquad Y_1(t) = \frac{\lambda}{\delta + \alpha_1} - \frac{\delta}{\beta_1} + \eta(t),$$

$$\xi(0) = \xi_0, \quad \eta(0) = \eta_0.$$

- Can approximate the fixation probability; get correction of the form

$$-\frac{\mathfrak{R}_{0,1}(\delta + \alpha_2)\eta_0}{\lambda\mathfrak{R}_{0,1} - \delta}\left(1 - \frac{\mathfrak{R}_{0,1}}{\mathfrak{R}_{0,2}}\right) + \mathcal{O}\left(\left(1 - \frac{\mathfrak{R}_{0,1}}{\mathfrak{R}_{0,2}}\right)^2\right)$$

- Recalling that $\mathfrak{R}_{0,1} > \frac{\delta}{\lambda}$, we see that this is an decreasing function of α_2 if $\eta_0 > 0$ and increasing if $\eta_0 < 0$, where we recall that η_0 is the perturbation in the density of individuals infected with the wild-type strain 1.
- Increasing virulence increases the fixation probability when the number of the wild-type is below equilibrium levels, and decreases it when the wild-type is above the equilibrium level.
- Note that the virulence of each of the two strains appears, independent of $\mathfrak{R}_{0,i}$.

ADAPTIVE DYNAMICS FOR THE TWO STRAIN SIR MODEL

We can consider the long term evolution of the virulence in the framework of
adaptive dynamics: we assume that

- With rate $\nu_n \ll \frac{1}{n \ln n}$, an infected host transmits a novel mutant strain;
  this scaling ensures that with high probability, fixation occurs before a
  second novel mutation can arise.
- Mutations have small effects, and are unbiased in direction, so that a
  strain of virulence α gives rise to a new strain of virulence α' according
  to a kernel $K(\alpha, \alpha')$ with mean 0, variance $\varepsilon\sigma^2(\alpha)$, and higher moments
  of order $o(\varepsilon)$, and
- The transmissibility of the strain depends on the virulence according to
  some fixed function $\beta(\alpha)$.
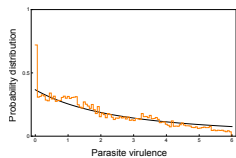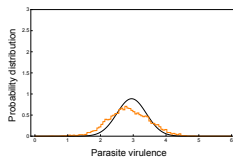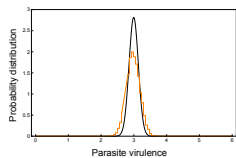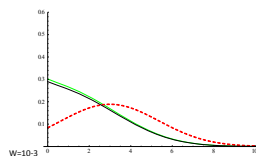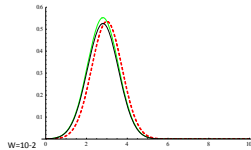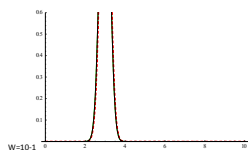- Here, the reproductive number is a function of the virulence:

$$\mathfrak{R}_0(\alpha) = \frac{\beta(\alpha)}{\delta + \alpha}.$$

CANONICAL DIFFUSION (CHAMPAGNAT & LAMBERT, 2007)

► Rescaling time by $\varepsilon \nu_n$ and passing to the limit $\varepsilon \to 0$, for large values of *n*, the population is w.h.p. monomorphic *i.e.,* all strains have the same variance – on this timescale, the fixation time is vanishingly small.

► The value of the virulence as a function of time, $A(t)$ obeys a diffusion process: we can use Laplace's method to obtain a simple expression for this distribution:

► Let $I_e(\alpha) = n\left(1 - \frac{\delta + \alpha}{\beta(\alpha)}\right)$.

► Letting $\alpha^\star$ be the value of α that maximises $\mathfrak{R}_0$, the stationary distribution is approximately

$$\left(\frac{\beta(\alpha^\star)}{\beta(\alpha)}\right)^2 \frac{1}{\sqrt{\frac{2\pi}{2I_e(\alpha^\star)\frac{|\beta''(\alpha^\star)|}{\beta(\alpha^\star)}}}} e^{-I_{eq}(\alpha^\star)\frac{|\beta''(\alpha^\star)|}{\beta(\alpha^\star)}(\alpha-\alpha^\star)^2}$$

$$\beta(\alpha) = (\delta + \alpha)(\beta_{max} - w(\alpha - \alpha^\star)^2)$$

Parameters: $n = 500$, $\beta_{max} = 10$, $\delta = 3$, $\alpha^\star = 3$

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CONCLUSIONS

► Looking at escape from the boundary is a natural problem in evolutionary models.

► The class of density dependent population processes admit a natural branching process approximation in the boundary: the resident species are approximated by their law of large numbers deterministic limit, the invaders are modelled by a branching process with time dependent rates.

► The boundary Lyapunov exponent plays the role of the Mathusian parameter for the branching process - leads to potential links with work on permanence in dynamical systems.

► The branching process allows us to obtain simple asymptotic expressions for fixation probabilities, times, *etc.* in models of biological interest.

► Further extensions(?): multiple invading types (multi-type branching processes), mutations (branching processes with immigration)

THANK YOU!