Approximations in Population Processes with high carrying capacity K.

Fima Klebaner, Monash University In Progress

Joint work with: Kais Hamza, Monash, Peter Jagers, Chalmers, Haya Kaspi, Technion.

Luminy, June, 2012.

- Outline

A population model, A_t^K , $t \ge 0$, (Markov, can be vector or measure valued) with parameters (reproduction, lifespan) dependent on K and the state of the population (say density, $|A_t|/K$). Bare Bones Evolution model in view Population (s) are in "equilibrium" near carrying capacity (s), then a new mutant appears that out competes in the beginning, then may co-exist or take over.

Example: Binary splitting with

$$p=\frac{K}{K+|A|}.$$

- 1. Initial conditions are in the vicinity of K (say $|A_0^K| = dK$)
- 2. Initial conditions do not depend on K (say $|A_0^K| = 1$)

Outline

- Approximations

If parameters stabilize as $K \to \infty$, and if there is smooth dependence on initial conditions, then we have $A_0^K \to A_0$, implies

$${\sf A}_t^{\sf K} o {\sf A}_t,$$
 as ${\sf K} o \infty$

(in distribution) on any finite time interval [0, T], where the limiting process has initial condition A_0 and dynamics determined by the limiting parameters.

Outline

Approximations

1. Initial conditions dK

Then $|A_0^{\mathcal{K}}| \to \infty$, and the approximation on finite time intervals does not apply.

In this case we have approximation to

$$\frac{1}{K}A_t^K \Rightarrow A_t^\infty,$$

LLN, or fluid approximation.

In this talk we show this for one type age-dependent process, which is Markov if considered as measure-valued.

We establish the weak convergence of the measure-valued processes $\{\frac{1}{K}A_t^K, t \ge 0\}_K$, in $D(R^+, \mathcal{M}(R^+))$ the Skorokhod space of all cadlag functions from R^+ to $\mathcal{M}(R^+)$ with its Skorokhod topology.

Outline

- Approximations

2. Problem of small initial size

We want to model the following situation. In the beginning there is only 1 new mutant that at first out competes the host population. Due to exponential growth it takes time of order log K to grow to dK, where LLN kicks in.

A feature of population model is that 0 is absorbing.

LLN gives convergence to the limiting process, that starts at 0, which is always 0.

The original approximation is also on finite times, but we need intervals $[0, T_K]$ with $T_K \to \infty$.

In the literature, people treat the process in two steps, rather than one.

Here we propose the time change that looks like $\log K + t$, or perhaps a random time of order $\log K$ plus t.

Outline

Approximations

An abstract problem of approximation of dynamical system with unstable fixed point, where the initial conditions converge to that fixed point.

Picture here.

Example.

The differential equation

$$\dot{x}_t^{\varepsilon} = x_t^{\varepsilon}, \ x_0^{\varepsilon} = \varepsilon.$$

has solution

$$x_t^{\varepsilon} = \varepsilon e^t.$$

So that on any time interval [0, T]

$$x_t^{arepsilon}
ightarrow 0, \;\; as, \;\; arepsilon
ightarrow 0.$$

But for $T_{\varepsilon} = -\log \varepsilon + t$, $x_{T_{\varepsilon}}^{\varepsilon} = e^{t}$. Hence it satisfies same dynamics but with a different initial condition.

- Description of the model with ages

Age-dependent model

Population of particles, who give birth during lifetime, then die after a random time. Upon death they leave a random number of offspring.

Parameters of the model:

- ▶ the death rate=hazard function h = G'/(1 G) (G is a lifespan distribution)
- reproduction rate b
- offspring distribution at splitting, mean offspring *m*, variance v².

Population is described at time *t* by the ages of all the particles, $A_t = (a_t^1, a_T^2, \dots, a_t^{Z_t}), Z_t = |A_t|.$ parameters *h*, *b*, *m* etc dependent on *A*.

Description of the model with ages

-Measure-valued Markov process of ages

A collection of individuals with ages $(a^1, \ldots, a^z) = A$. To deal with varying dimension, look at A as a measure, for a set B (of ages), A(B) counts the number of particles with ages in B,

$$A(B) = \sum_{i=1}^{z} \delta_{a_i}(B),$$

where $\delta_a(B)$, the point measure at *a*.

When there are no births and deaths the population is changing only by ageing.

When a particle is born a point mass appears at zero.

When a particle dies its point mass disappears and offspring number of point masses at zero appear.

Description of the model with ages

Measure-valued Markov process of ages

3. The generator of A_t

We use notations $\mathcal{M}(R^+)$ the space of finite, positive measures on R^+ , equipped with weak topology. For $A \in \mathcal{M}(R^+)$ $(f, A) = \int f(x)A(dx)$ If A is concentrated on points

$$(f,A)=\sum_{i=1}f(a^i).$$

For $A_t = (a_t^1, \ldots, a_t^{z_t})$ the population size $Z_t = (1, A_t)$. The class of functions we use is of the form F((f, A)), where F is a function on R.

Description of the model with ages

Measure-valued Markov process of ages

3 cont. The generator of A_t

Theorem. [JK00] For a bounded differentiable function F on R and a continuously differentiable function f on R^+ , the following limit exists

$$\lim_{t\to 0}\frac{1}{t}\mathbb{E}_{\mathcal{A}}\Big\{F((f,A_t))-F((f,A))\Big\}=\mathcal{G}F((f,A)),$$

where

$$\mathcal{GF}((f,A)) = F'((f,A))(f',A) + \sum_{j=1}^{z} b_{A}(a^{j}) \{F(f(0) + (f,A)) - F((f,A))\}$$

$$+\sum_{j=1}^{2}h_{A}(a^{j})\{\mathbb{E}_{A}[F(Y(a^{j})f(0)+(f,A)-f(a^{j}))]-F((f,A))\},$$

and Y(a) denotes the number of children at death of a mother, dying at age *a*.

- Description of the model with ages

Measure-valued Markov process of ages

4. Itô's formula

Consequently, Itô's formula holds: for a bounded C^1 function F on R and a C^1 function on R^+

$$F((f, A_t)) = F((f, A_0)) + \int_0^t \mathcal{G}F((f, A_s))ds + M_t^{F, f},$$

where $M_t^{F,f}$ is a local martingale

$$\left\langle M^{F,f}, M^{F,f} \right\rangle_t$$

$$=\int_0^t \left[\mathcal{G}F^2((f,A_s))ds-2F((f,A_s))\mathcal{G}F((f,A_s))\right]ds.$$

Description of the model with ages

Measure-valued Markov process of ages

Itô's formula for (f, A_t) By taking F(u) = u and u^2 (justification by stopping), for $f \in C^1(R^+)$

$$(f, A_t) = (f, A_0) + \int_0^t (L_{A_s}f, A_s)ds + M_t^f,$$

where the linear operators L_A are defined by

$$L_A f = f' - h_A f + f(0)(b_A + m_A h_A),$$

and M_t^f is a local square integrable martingale with

$$\left\langle M^{f}, M^{f} \right\rangle_{t} = \int_{0}^{t} \left(f^{2}(0) v_{A_{s}}^{2} h_{A_{s}} + h_{A_{s}} f^{2} - 2f(0) m_{A_{s}} h_{A_{s}} f, A_{s} \right) ds.$$

 $m_A(u)$ is the mean and $v_A(u)$ is the second moment of the offspring-at-splitting distribution when population is A_{A}

Description of the model with ages

Measure-valued Markov process of ages

6. Itô's formula with a true martingale.

Theorem. [JK00] if $f \ge 0$ satisfies the (linear growth) condition (H1)

$$|(L_A f, A)| \le C(1 + (f, A))$$
 (H1)

for some C > 0 and any A, and if (f, A_0) is integrable, then (f, A_t) is integrable and

$$\mathbb{E}[(f,A_t)] \leq \left(\mathbb{E}[(f,A_0)] + Ct\right) \left(1 + \frac{1}{C}e^{Ct}\right).$$

Moreover, M_t^f is a martingale. Proof. Gronwall with localization.

Description of the model with ages

- Measure-valued Markov process of ages

7. Sufficient conditions for (H1)

A set of functions is *uniformly bounded* if the set of all functions vales is bounded.

Corollary. If the birth and death intensities, b_A , h_A and the mean at splitting m_A , are all uniformly bounded and the functions f and f' are bounded, then the growth condition (H1) is satisfied. Call this condition (C0).

In particular, the function identically 1 satisfies condition (H1) so that

$$\mathbb{E}[|A_t|] \leq \left(\mathbb{E}[|A_0|] + Ct\right) \left(1 + \frac{1}{C}e^{Ct}\right).$$

Further, if the $v_A, A \in \mathcal{M}(R^+)$) are uniformly bounded, then M_t^f is a square integrable martingale with quadratic variation

$$\left\langle M^{f}, M^{f} \right\rangle_{t} \leq C \int_{0}^{t} |A_{s}| ds.$$

Description of the model with ages

- Measure-valued Markov process of ages

8. Processes with carrying capacity K

Now the carrying capacity K enters and we consider processes $\{A_t^K, t \ge 0\}_K$, where K is a parameter, as a collection of measure-valued processes. Parameters of the processes (the functions $h_{A^K}^K$, $b_{A^K}^K$, $m_{A^K}^K$) may also depend upon K. Then, A_t^K is a random function on R^+ with values in $\mathcal{M}(R^+)$, the space of finite, positive measures on R^+ , equipped with its weak topology.

Description of the model with ages

Measure-valued Markov process of ages

9. Weak convergence

- ► D(R⁺, M(R⁺)) is the Skorokhod space of all cadlag functions from R⁺ to M(R⁺) with its Skorokhod topology.
- ▶ We establish the weak convergence of the measure-valued processes $\{\frac{1}{K}A_t^K, t \ge 0\}_K$, writing bar $\bar{A}_t^K = \frac{1}{K}A_t^K$ in $D(R^+, \mathcal{M}(R^+))$.
- ► We show that their distributions, which are the corresponding measures on D(R⁺, M(R⁺)), say Q^K, converge to a limit measure Q.

• Q corresponds to (non-random) limit A^{∞} .

Description of the model with ages

- Measure-valued Markov process of ages

10. Establishing weak convergence

Weak convergence, by definition is convergence of the expectations of bounded and continuous functionals. Since practically it is impossible to check,

one way to establishing weak convergence of measures is to show

- SC Sequential compactness. From every sequence can extract a convergent subsequence.
 - U The limit is unique.

To show SC, in turn tightness is established.

By Prokhorov's theorem,

a collection of probability measures (on a separable metric space) is tight if and only if it is sequentially compact.

Description of the model with ages

Measure-valued Markov process of ages

12. Establishing Tightness

Theorem [Hamza Jagers K. 12]

Suppose that parameters are uniformly bounded. Suppose also that the expected total mass of $\frac{1}{K}A_0^K$ is bounded, $\sup_K \mathbb{E}[\frac{1}{K}|A_0^K|] < \infty$.

Then the family $\{\frac{1}{K}A_t^K, t \ge 0\}_K$ in $D(R^+, \mathcal{M}(R^+))$ is tight. Proof uses Jakubowski's criteria.

Description of the model with ages

-Measure-valued Markov process of ages

13. Jakubowski's criteria

A sequence μ^{K} of $D(R^{+}, \mathcal{M}(R^{+}))$ -valued random elements is tight if and only if the following two conditions are satisfied. J1. (Compact Containment) For each T > 0 and $\eta > 0$ there exists a compact set $C_{T,\eta} \in \mathcal{M}(R^{+})$ such that

$$\liminf_{K\to\infty} \mathbb{P}(\mu_t^K \in C_{T,\eta} \ \forall t \in [0, T]) > 1 - \eta.$$

J2. (Coordinate Tightness) There exists a family **F** of real continuous functions F on $\mathcal{M}(R^+)$ that separates points in $\mathcal{M}(R^+)$ and is closed under addition such that for every $F \in \mathbf{F}$, the sequence $\{F(A_t^K), t \in [0, \infty)\}$, is tight in $D(R^+, R)$.

Description of the model with ages

- Measure-valued Markov process of ages

14. Proof of Compact Containment

Note that for for metric spaces compactness and sequential compactness are equivalent. Since weak convergence is metrizable (Levy-Prokhorov metric), it is enough to have SC. For each T > 0 and $\eta > 0$ let

$$C_{\mathcal{T},\eta} = \{ \mu \in \mathcal{M}(\mathbb{R}^+) : \mu((\mathcal{T},\infty)) < j_\eta \},\$$

where $j_{\eta} = \sup_{K} \mathbb{E}[\frac{1}{K} |A_{0}^{K}|]/\eta$. First note that by the Portmanteau Theorem, if $\mu_{n} \in C_{T,\eta}$ and $\mu_{n} \Rightarrow \mu$ then $\liminf \mu_{n}((T,\infty)) \ge \mu((T,\infty))$. Therefore $\mu \in C_{T,\eta}$. Since the space is metric, sequential compactness implies compactness.

Description of the model with ages

Measure-valued Markov process of ages

Proof of Compact Containment

Second, observe that if an individual at time $t \leq T$ has an age greater than T, it must have been present at time 0. In other words, for all $t \leq T A_t^K((T,\infty)) \leq |A_0^K|$. Hence,

$$\mathbb{P}\left(\frac{A_t^K}{K} \in C_{\mathcal{T},\eta} \; \forall t \in [0, T]\right) = \mathbb{P}\left(\frac{A_t^K((\mathcal{T}, \infty))}{K} < j_\eta \; \forall t \in [0, T]\right)$$
$$\geq \mathbb{P}\left(\frac{|A_0^K|}{K} < j_\eta\right) = 1 - \mathbb{P}\left(\frac{|A_0^K|}{K} \ge j_\eta\right)$$

by Chebyshev's ineq. and choice of $j_{\eta} = \sup_{K} \mathbb{E}[\frac{1}{K} |A_{0}^{K}|]/\eta$

$$\geq 1 - \sup_{\mathcal{K}} \mathbb{E}[rac{|\mathcal{A}_0^{\mathcal{K}}|}{\mathcal{K}}]/j_\eta \geq 1 - \eta$$

Description of the model with ages

- Measure-valued Markov process of ages

15. Proof of Coordinate Tightness

Consider the family of real-valued functions **F** on $\mathcal{M}(R^+)$, by

$$\mathbf{F} = \{F : \exists f \in C_b^1(R^+) \text{ with } f' \text{ bounded} : F(\mu) = (f, \mu)\}.$$

Every function in **F** is continuous with respect to the weak topology on $\mathcal{M}(R^+)$, the class **F** is trivially closed with respect to addition, and it separates points in $\mathcal{M}(R^+)$. Enough to show that for any $f \in \mathbf{F}$, the sequence of real valued processes $X_t^K = (f, \frac{1}{K}A_t^K)$ is tight in the $D(R^+, R)$. This is a standard problem for semimartingales and is done by use of Aldous's criterion for tightness in $D(R^+, R)$.

Description of the model with ages

Measure-valued Markov process of ages

16. Aldous's criterion

For any T > 0 and stopping time τ (actually τ^{K} , but the dependence upon K implicit) and any bounded $f \ge 0$, it must be checked that

$$\lim_{j\to\infty}\limsup_{K}\mathbb{P}(X_T^K>j)=0,$$

and

$$\lim_{\delta\to 0}\limsup_{K}\sup_{\tau<\tau-\delta}\mathbb{P}(\sup_{t\leq\delta}|X_{\tau+t}^{K}-X_{\tau}^{K}|>\varepsilon)=0, \ \forall \varepsilon>0.$$

This is done by using the basic integral representation for the process and bounds.

Description of the model with ages

C2)

Measure-valued Markov process of ages

Assumption on stabilization of parameters: demographical smootheness

C1) Assume that there is a Lipschitz continuous function m^{∞} defined on $\mathcal{M}(R^+)$, such that

$$m_A^K = m_{\frac{1}{K}A}^\infty,$$

$$|m_A^{\infty}-m_B^{\infty}|\leq C\rho(A,B),$$

where $\rho(A, B)$ is the Levy-Prokhorov distance.

. .

There are functions h^{∞} , and b^{∞} defined on $\mathcal{M}(R^+) \times R^+$ which are Lipschitz continuous in the first argument, s.t.

. .

$$h_{A}^{K}(u) = h_{\frac{1}{K}A}^{\infty}(u), \quad b_{A}^{K}(u) = b_{\frac{1}{K}A}^{\infty}(u),$$
$$\parallel h_{A}^{\infty} - h_{B}^{\infty} \parallel \leq C\rho(A, B), \quad \parallel b_{A}^{\infty} - b_{B}^{\infty} \parallel \leq C\rho(A, B).$$
C2) Initial populations stabilise, $\frac{1}{K}A_{0}^{K} \Rightarrow \bar{A}_{0}$, and $\sup_{K} \mathbb{E}[|A_{0}^{K}|]/K < \infty.$

Description of the model with ages

- Measure-valued Markov process of ages

Fluid limit (LLN).

Theorem [Hamza Jagers K. 12] Assume conditions C0, C1 and C2. Then the processes $\frac{1}{K}A^{K}$ converge weakly in $D(R^{+}, \mathcal{M}(R^{+}))$. The limiting measure \bar{A}_{t}^{∞} , displays no randomness beyond that possibly in \bar{A}_{0}^{∞} . For any test function f, and any t > 0, it satisfies the integral equation

$$(f, A_t) = (f, \bar{A}_0^\infty) + \int_0^t (L_{A_s}^\infty f, A_s) ds,$$
 (1)

where

$$L^{\infty}_A f = f' - h^{\infty}_A f + f(0)(b^{\infty}_A + h^{\infty}_A m^{\infty}_A).$$

Further, \bar{A}_t^{∞} is absolutely continuous with respect to $\bar{A}_0 + \delta_0$, the latter being a mass point at zero. If \bar{A}_0 has a density with respect to Lebesgue measure on $(0, \infty)$, then so has \bar{A}_t^{∞} .

Description of the model with ages

Measure-valued Markov process of ages

18. Remarks

Remark. The limit equation is the weak form of the McKendrick-von Foerster equation for the density of A_t , a(t, x)

$$\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial u}\right)a(t,u)=-a(t,u)h_{A_t}(u),a(t,0)=\Big(\int_0^\infty m_{A_t}h_{A_t}(u)a(t,u)du\Big).$$

Of course, smoothness of the density must also be proved. *Remark.*

For the birth-and-death case with a fixed birth rate *b*, Tran gives an argument for absolute continuity building upon a relation $(\phi, A_t) \leq (\phi(t + \cdot), A_0) + \int_0^t (\phi(t - s)b, A_s) ds.$

Description of the model with ages

- Measure-valued Markov process of ages

19. Proof of convergence

Thanks to the Lipschitz assumption on the demographic parameters and Gronwall's inequality, the equation for the limit has a unique solution.

Since we already established tightness, it follows that any subsequence converges to the same limit, hence the whole sequence converges.

If $f \ge 0$ but $f' \le 0$, then a solution of (1) satisfies

$$(f, A_t) \leq (f, A_0) + f(0) \int_0^t (b_{A_s} + h_{A_s} m_{A_s}, A_s) ds \leq (f, A_0) + C(f, \delta_0).$$

Since this is true for all such f, it follows that A_t is absolutely continuous with respect to $A_0 + \delta_0$. If the former has a density with respect to Lebesgue measure on $(0, \infty)$, then so has A_t .

Description of the model with ages

Measure-valued Markov process of ages

Change of time

The population size will reach a level dK after time of order log K, due to exponential growth (unless of course it dies out). Let $T_{dK} = \inf\{t; Z_t \ge dK\}.$

Theorem (HJK-2012)

If $|A_0^K| = 1$ and previous conditions on parameters hold then $\bar{A}_{T_{dK}+t}$ converges to a limit that satisfies the same equation but with a different initial condition.

-Bare Bones Stochastic Equations

The resident population, which assumed to be around its carrying capacity, evolves as a binary splitting process with probability of successful reproduction (division) dependent on the size of that population Z^1 and also the size of the new mutant population Z^2 . The mutant populations also evolves as a binary splitting with initially very high probabilities of successful division. These probabilities are given below. Here ξ^1 and ξ^2 denote the generic random variables representing offspring distribution of the resident and the mutant populations. The population size is denoted by $\mathbf{Z} = (Z^1, Z^2)$.

Bare Bones Stochastic Equations

$$\begin{split} \mathbf{P} \left(\xi^{(1)} = 0 \,|\, \mathbf{Z} \right) &= \frac{Z^{(1)} + \gamma Z^{(2)}}{a_1 K + Z^{(1)} + \gamma Z^{(2)}}, \\ \mathbf{P} \left(\xi^{(1)} = 2 \,|\, \mathbf{Z} \right) &= \frac{a_1 K}{a_1 K + Z^{(1)} + \gamma Z^{(2)}}, \end{split}$$

and

$$\begin{split} \mathbf{P}\left(\xi^{(2)} = 0 \,|\, \mathbf{Z}\right) &=\; \frac{\gamma Z^{(1)} + Z^{(2)}}{a_2 K + \gamma Z^{(1)} + Z^{(2)}}, \\ \mathbf{P}\left(\xi^{(2)} = 2 \,|\, \mathbf{Z}\right) &=\; \frac{a_2 K}{a_2 K + \gamma Z^{(1)} + Z^{(2)}}. \end{split}$$

Bare Bones Stochastic Equations

- birth-death formulation

In a corresponding birth-death process the probability splitting into two gives the birth rate, and the complimentary probability the death rate. Hence individual death and birth rates are

$$\begin{split} \mu^1(z^1,z^2) &= C_1(z^1+\gamma z^2) \quad , \quad \lambda^1(z^1,z^2) = C_1 a_1 \mathcal{K}, \\ \mu^2(z^1,z^2) &= C_2(\gamma z^1+z^2) \quad , \quad \lambda^2(z^1,z^2) = C_2 a_2 \mathcal{K}, \end{split}$$

where C_1 , C_2 are constants. There is no unique translation to continuous time, but if we replace the unit of discrete time by the exponential waiting time with rate 1, then the birth and death rates add up to one. In this way the birth rate is exactly the splitting probability and the death rate is its complimentary probability.

Bare Bones Stochastic Equations

birth-death formulation

Hence in the first population individual birth and death rates are

$$\lambda^{1}(z^{1}, z^{2}) = \frac{a_{1}K}{a_{1}K + z^{(1)} + \gamma z^{(2)}}, \ \mu^{1}(z^{1}, z^{2}) = \frac{z^{(1)} + \gamma z^{(2)}}{a_{1}K + z^{(1)} + \gamma z^{(2)}}.$$

The rates in the whole populations are

$$z^1\lambda^1(z^1,z^2)$$
 and $z^1\mu^1(z^1,z^2)$.

(日) (日) (日) (日) (日) (日) (日) (日)

For the second population it is similar.

Bare Bones Stochastic Equations

-birth-death formulation

If X(t) is a Markov jump process with a positive holding time parameter a(x), the jump from x with mean m(x) and second moment v(x) then

$$X(t) = X(0) + \int_0^t a(X(s))m(X(s))ds + M(s),$$

where M(s) is a martingale with predictable quadratic variation

$$\langle M,M\rangle_s=\int_0^ta(X(s))v(X(s))ds.$$

In a Birth-Death process the holding parameter is $a(x) = \lambda(x) + \mu(x)$, where $\lambda(x)$ and $\mu(x)$ are birth and death rates of the population at x, i.e. at x the process stays for an exponentially distributed time with parameter a(x) then jumps to the state $x + \xi(x)$, where

$$\xi(x) = egin{cases} 1, & ext{with prob } \lambda(x)/a(x) \ -1, & ext{with prob } \mu(x)/a(x) \end{pmatrix}$$

Bare Bones Stochastic Equations

-birth-death formulation

Therefore we have the following representation for Z^1 (for Z^2 is similar)

$$Z_{t}^{1} = Z_{0}^{1} + \int_{0}^{t} \frac{a_{1}K - Z_{s}^{1} - \gamma Z_{s}^{2}}{a_{1}K + Z_{s}^{(1)} + \gamma Z_{s}^{(2)}} Z_{s}^{1} ds + M_{t}^{1}$$

$$Z_{t}^{2} = Z_{0}^{2} + \int_{0}^{t} \frac{a_{2}K - \gamma Z_{s}^{1} - Z_{s}^{2}}{a_{2}K + \gamma Z_{s}^{(1)} + Z_{s}^{(2)}} Z_{s}^{2} ds + M_{t}^{2}, \quad (3)$$

where

$$\langle M^1, M^1 \rangle_t = \int_0^t Z^1_s ds, \ \langle M^2, M^2 \rangle_t = \int_0^t Z^2_s ds.$$

Note that these processes are indexed by K, which is implicit, but when it is necessary we make it explicit. We would like to give an approximation for **Z** for large values of K.

Bare Bones Stochastic Equations

- Fluid approximation

Let $X_t^i = Z_t^i/K$. Then X_t^i has representation as dynamics plus a small noise for large K. Classical fluid approximation is given by a result of Kurtz (1970) [?].

Theorem

If $X_0^i \to x_0^i$ then (X_t^1, X_t^2) converges in sup norm on any finite time interval [0, T] to (x^1, x^2) defined a solution to the following system of equations

$$x_{t}^{1} = x_{0}^{1} + \int_{0}^{t} \frac{a_{1} - x_{s}^{1} - \gamma x_{s}^{2}}{a_{1} + x_{s}^{(1)} + \gamma x_{s}^{(2)}} x_{s}^{1} ds,$$

$$x_{t}^{2} = x_{0}^{2} + \int_{0}^{t} \frac{a_{2} - \gamma x_{s}^{1} - x_{s}^{2}}{a_{2} + \gamma x_{s}^{(1)} + x_{s}^{(2)}} x_{s}^{2} ds.$$
(4)

Bare Bones Stochastic Equations

-Fluid approximation

Fixed points of the deterministic system The system (4) has four fixed points, obtained by solving the system

$$(x_t^1)' = 0, \ (x_t^2)' = 0.$$

They are: (0,0), $(0,a_2)$, $(a_1,0)$ and

$$(x_1^*, x_2^*) = \left(\frac{a_1 - \gamma a_2}{1 - \gamma^2}, \frac{a_2 - \gamma a_1}{1 - \gamma^2}\right).$$
 (5)

The parameters are chosen in such a way that $a_i > 0$, $0 < \gamma < 1$, $a_1 - \gamma a_2 > 0$ and $a_2 - \gamma a_1 > 0$, so that the last point is the only one in the positive quadrant.

The first three fixed points are unstable, and (x_1^*, x_2^*) is stable, and we shall see that solutions converge to it from any positive initial condition.

Bare Bones Stochastic Equations

-Fluid approximation

Convergence to unstable fixed point.

In the Evolution model the initial number of new mutants is one, $Z_0^2 = 1$, while the initial number of the resident population is around its carrying capacity K. Thus $X_0^2 = 1/K$ and its limit as $K \to \infty$ is $x_0^2 = 0$.

Thus it follows from Theorem 2 that the fluid approximation for the Evolution Model on any fixed time interval is the unstable fixed point $(a_1, 0)$.

◆□ ▶ < 圖 ▶ < 圖 ▶ < 圖 ▶ < 圖 • 의 Q @</p>

Bare Bones Stochastic Equations

Fluid approximation

Pictures

Bare Bones Stochastic Equations

-Fluid approximation

Let $T_K = \inf\{t : x_t^2 = \alpha\}$. The change of time is $T_K + t$. We need to show that $x^1(T_K + t)$ converges as $K \to \infty$. This is done by writing x^1 as a function of x^2 (these are monotone), and showing that solution to these equations converge.

Bare Bones Stochastic Equations

- Fluid approximation

Differential equations for the time changed system $\tau_x = (x^2)^{-1}(x)$ For any t in the range of x^2 , $t \in [1/K, x_2^*)$

$$x^2(\tau_t)=t,$$

dependence on K only in the range of x^2 , $x^2([0,\infty)) = [1/K, x_2^*)$. $y^K(t) = x^1(\tau_t)$ is given by

$$(y^{\kappa})'(t) = F(t, y^{\kappa}(t)), \ 1/\kappa \le t < x_2^*, \ y^{\kappa}(\frac{1}{\kappa}) = x^1(0) = a_1,$$
(6)

with

$$F(t,y) = \frac{(a_1 - t\gamma - y)y(a_2 + t + \gamma y)}{t(a_1 + t\gamma + y)(a_2 - t - \gamma y)}.$$
(7)

Bare Bones Stochastic Equations

- Fluid approximation

Theorem (Hamza Kaspi K)

The sequence $y^{K}(t)$ on [0, d] converges as $K \to \infty$ to the unique solution of the differential equation

$$y'(t) = F(t, y(t)), t > 0, y(0) = a_1.$$
 (8)

This equation is extended to t = 0 by defining $F(0, a_1)$ by continuity.

$$F(0,a_1)=\frac{-\gamma(a_2+\gamma a_1)}{2(a_2-\gamma a_1)}.$$

Bare Bones Stochastic Equations

-Fluid approximation

Proof

The key is to decompose F as follows

$$F(t,y) = H(t,y)\Pi(t,y), \qquad (9)$$

$$H(t,y) = \frac{(a_1 - y - \gamma t)}{t}, \qquad (10)$$

$$\Pi(t,y) = \frac{y(a_2+t+\gamma y)}{(a_1+\gamma t+y)(a_2-\gamma y-t)}.$$
 (11)

 Π is bounded, Lipschitz, all the nasties are in *H*. But *H* is linear, so can solve explicitly.

For a fixed small d > 0 ($d < a_2 - \gamma a_1$), there are two positive constants \overline{C} and \underline{C} such that for all $0 \le t \le d$

$$\underline{C} \leq \Pi(t, y^{K}(t)) \leq \overline{C},$$

Bare Bones Stochastic Equations

Fluid approximation

Hence we obtain that y^{K} is bounded by solutions of linear differential equation: for $1/K \le t \le d$

$$a_1+ar{C}\int_{1/K}^t H(s,y^K(s))ds\leq y^K(t)\leq a_1+ar{C}\int_{1/K}^t H(s,y^K(s))ds.$$

-Bare Bones Stochastic Equations

Fluid approximation

Lemma Let y(t) solve the ode on $[t_0, d]$,

$$y'(t)=crac{a-y(t)-\gamma t}{t},\ y(t_0)=a.$$

Then the only solution is given by the function

$$y(t) = a - rac{c\gamma}{c+1} \Big(t - rac{t_0^{c+1}}{t^c}\Big).$$

(日) (日) (日) (日) (日) (日) (日) (日)

When $t_0 = 0$, y(t) is linear.

Bare Bones Stochastic Equations

- Fluid approximation

Next show that $y^{\kappa}(t)$ is sequentially compact. As the functions $y^{\kappa}(t)$ are monotone and bounded, existence of a convergent subsequence is assured by the Helly-Bray lemma. The limit function y(t) is monotone and has at most countably many jump discontinuities. Write the integral equation for $y^{\kappa}(t)$

$$y^{K}(t) = a_{1} + \int_{0}^{t} \mathbb{1}_{[\frac{1}{K},d]}(s)F(s,y^{K}(s))ds.$$
 (12)

Uniqueness is shown also using corresponding linear equation (by taking $y_1 - y_2$ not $|y_1 - y_2|$!) The same as in

$$y' = -\frac{y}{t}, \ y(0) = 0.$$

Bare Bones Stochastic Equations

- Fluid approximation

The system with the new time is given by

$$\mathbf{x}^{K}(T_{K}+t) = \mathbf{x}^{K}(0) + \int_{0}^{T_{K}+t} \mathbf{G}(\mathbf{x}^{K}(s)) ds,$$

with

$$\mathbf{x}^{K}(0) = \begin{pmatrix} a_{1} \\ \frac{1}{K} \end{pmatrix},$$

 $\mathbf{G}(\mathbf{x})$ is a vector function of two variables $\mathbf{G}(\mathbf{x}) = \begin{pmatrix} g_1(\mathbf{x}) \\ g_2(\mathbf{x}) \end{pmatrix}$. Change variable $s = u + T_K$, for the time changed system

$$\mathbf{x}^{K}(T_{K}+t) = \mathbf{x}^{K}(0) + \int_{0}^{T_{K}} \mathbf{G}(\mathbf{x}^{K}(s))ds + \int_{0}^{t} \mathbf{G}(\mathbf{x}^{K}(T_{K}+u))du$$
$$= \begin{pmatrix} x^{K}(T_{K}) \\ \alpha \end{pmatrix} + \int_{0}^{t} \mathbf{G}(\mathbf{x}^{K}(\tau^{K}(u)))du.$$

Thus the time-changed system satisfies the same dynamics **G** with different initial conditions $x^1(T_K)$ and $x^2(T_K) = \alpha_{\text{conditions}} = \alpha_{\text{conditii}} = \alpha_{\text{$

Bare Bones Stochastic Equations

Fluid approximation

Corollary. For the deterministic system there exists

$$\lim_{K\to\infty} \mathbf{x}^K (T_K + t) = \mathbf{x}_{\alpha}(t),$$

that uniquely solves

$$\mathbf{x}_{lpha}(t) = \left(egin{array}{c} y(lpha) \ lpha \end{array}
ight) + \int_{0}^{t} \mathbf{G}(\mathbf{x}_{lpha}(u)) du.$$

this system converges to the stable fixed point.

-Fluid Approximation for the time-changed stochastic system

Let $X_t^i = Z_t^i / K$. Denote this process by \mathbf{X}_t^K and its martingale by \mathbf{M}_t^K , and by \mathbf{x}_t^K the solution of the corresponding deterministic system with same initial conditions.

$$\mathbf{X}_{T_{K}+t}^{K} = \mathbf{X}_{T_{K}}^{K} + \int_{0}^{t} \mathbf{G}(\mathbf{X}_{T_{K}+s}^{K}) ds + \frac{1}{K} \Big(\mathbf{M}_{T_{K}+t}^{K} - \mathbf{M}_{T_{K}}^{K} \Big).$$

By looking at quadratic variation the martingale term vanishes in the limit.

Theorem (Hamza Kaspi K.)

The sequence of processes $\mathbf{X}_{T_{K}+t}^{K}$ converges in probability in sup norm as $K \to \infty$, on any finite time interval [0, T], to the unique solution $\mathbf{x}(t)$ of the deterministic system

$$\mathbf{x}(t) = \begin{pmatrix} W_1 \\ W_2 \end{pmatrix} + \int_0^t \mathbf{G}(\mathbf{x}(u)) du,$$

with $W_i = \lim_{K \to \infty} \frac{1}{K} Z^i_{T_K}$.

-Fluid Approximation for the time-changed stochastic system

Sketch of proof.

The main work is in proving convergence of $\mathbf{X}_{T_{K}}^{K} = \frac{1}{K} \mathbf{Z}_{T_{K}}^{K}$. Use that for the BD processes with such rates, as $t \to \infty$, there is convergence a.s. and in L^{2} (Kle on growth of processes with asymptotically linear rate of change, JAP, 1994).

$$W^K_t=e^{-t}Z^K_t o W^K, \ t o\infty.$$

Write equation for W_t^K (using by parts) and put $t = T_K$ From eq. (3) the drift term $\Lambda(\mathbf{z}) = \mathbf{z} + D(\mathbf{z})$ with $D_1(\mathbf{z}) = -\frac{2(z_1+\gamma z_2)}{a_1K+z_1+\gamma z_2}$, D_2 similar

$$W_{T_{\kappa}}^{K} = W_{0}^{K} + \int_{0}^{T_{\kappa}} e^{-s} D(Z_{s}^{K}) ds + \frac{1}{K} \int_{0}^{T_{\kappa}} e^{-s} dM_{s}^{K}.$$

-Fluid Approximation for the time-changed stochastic system

References

- Champagnat N.. Ferrière R., and Méléard S. (2007) Individual-based probabilistic models of adaptive evolution and various scaling approximations. *Progress in Probability* 59 (2007), 75-113, Birchhauser, Basel.
- Champagnat N.. Ferrière R., and Méléard, S. (2008) From individual stochastic processes to macroscopic models in adaptive evolution. *Stochastic Models* 24, 244.
- Champagnat N, Méléard S. (2011) Polymorphic evolution sequence and evolutionary branching. *Probab. Theory Relat. Fields*, 151:45–94.
- Hamza K. and Klebaner F.C. (1995) Conditions for integrability of Markov chains. J. Appl. Prob. 32, 541-547.
- Jagers P and Klebaner F.C. (2000) Population-Size-Dependent and Age-Dependent Branching Processes. Stochastic Processes and Their Applications 87, 235-254.

-Fluid Approximation for the time-changed stochastic system

- Jagers P. and Klebaner F.C. (2011) Population size dependent, age structured branching processes linger around their carrying capacity. J. Appl. Prob. 48A, 249-260.
- Jakubowski A. (1986) On the Skorokhod topology. Ann. Inst. H. Poincaré B22, 263-285.
- Kaspi H. and Ramanan K. Law of Large Numbers Limits for Many-Server Queues. (2011) Ann. Appl. Prob. 21(1), 33-114.
- Klebaner F. C. (1994) Asymptotic Behaviour of Markov Population Processes with Asymptotically Linear Rate of Change. JAP, 31, 614-625.
- Klebaner F. C., Sagitov S., Vatutin V.A., Haccou P, and Jagers P. (2011) Stochasticity in the adaptive dynamics of evolution: the bare bones. J. Biol. Dyn. 5, 147-162.
- Méléard S. and Tran V. C. (2012) Slow and fast scales for superprocess limits for age-structured populations. *Stoch. Proc. Applic.* 122, 250-276.

-Fluid Approximation for the time-changed stochastic system

 Tran, V. C. Large population limit and time behaviour of a stochastic particle model describing an-age-structured population. ESAIM: PS 12, 345-386 (2007)

MERCI BEAUCOUP

THANK YOU