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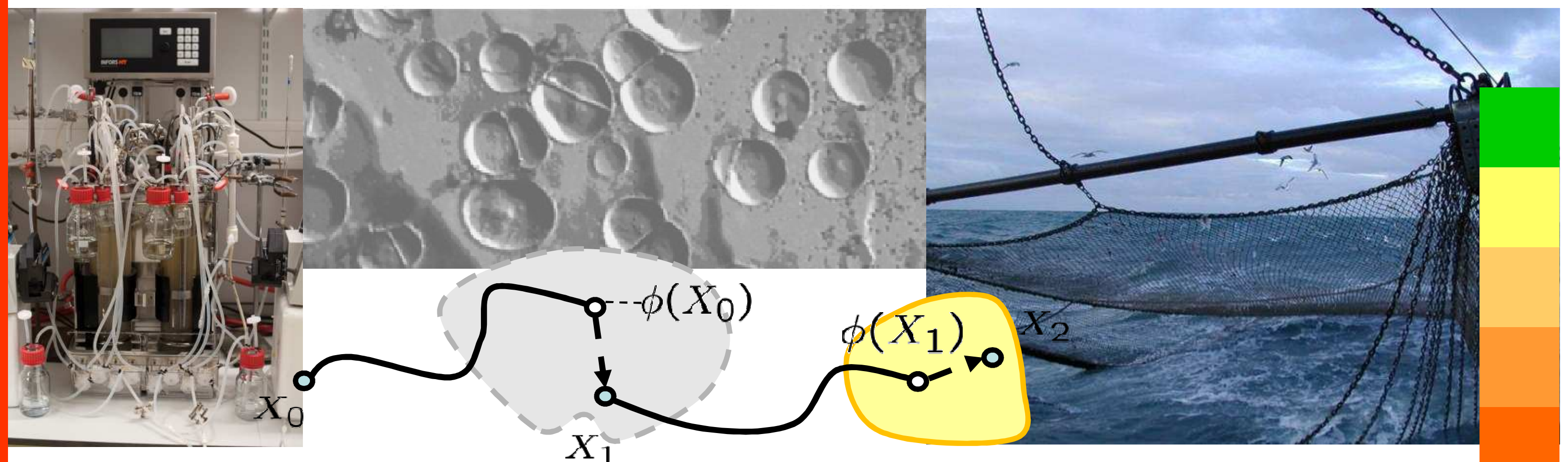
Towards understanding the role of noise in biological systems:

the long-term dynamics of deterministic systems perturbed by small random interventions



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Banach Center, Bedlewo, 21th June 2013

Outline of lecture

Part I:

Biological / experimental background and motivation

Related experimental research questions

Mathematical modeling

Brief discussion of applicable analysis frameworks

Part II:

Mathematical preliminaries

Discussion of the mathematical analysis

Part I

Biological-experimental
background and motivation

Noise in biological systems:

Main view has been

Organisms, especially small sized, e.g. unicellular, must deal with the nuisance of noise

i.e. preventing side effects: **robustness**

– **Intrinsic noise**:
originating from the 'design' of the biochemical cellular system, caused by small molecular numbers, thermodynamic fluctuations
e.g. *regulation*: single (large) DNA molecule, few-to-one interaction…

– **Extrinsic noise**:
originating from the unpredictability, randomness in the environment, having effects on the organism

Noise in biological systems:

New complementary view is developing

Organisms may exploit noise to increase their competitivity as species

i.e. intrinsic noise in the system has a **function** too, in specific cases.

1.) Mathematical modeling and analysis is required to get further understanding of the extent of effects caused by noise in biological systems.

2.) Understand mathematically to what extent the behaviour of deterministic models of biosystems are changed when random effects are added.

Part I

3 types of motivating examples

A.) Random interventions at fixed times

B.) Deterministic interventions at random times

C.) Random interventions at random times

Part I

3 types of motivating examples

A.) Random interventions at fixed times

(B.) Deterministic interventions at random times)

(C.) Random interventions at random times)

Motivating examples

Some motivation comes from experimental work on bacteria

in the interdisciplinary applied research project in the Netherlands

BetNet: **'Bet**-hedging **Net**works'

funded by the Dutch funding agency for scientific research NWO

'The evolution of stochastic heterogeneous networks as bet-hedging adaptations to fluctuating environments'

Oscar Kuipers
Jeroen Siebring
(Microbiology group, Rijksuniversiteit Groningen)

Patsy Haccou
Fátima Drubi
(Theoretical biology group, Leiden University)

Michael Emmerich
(Computer Science, Leiden University)

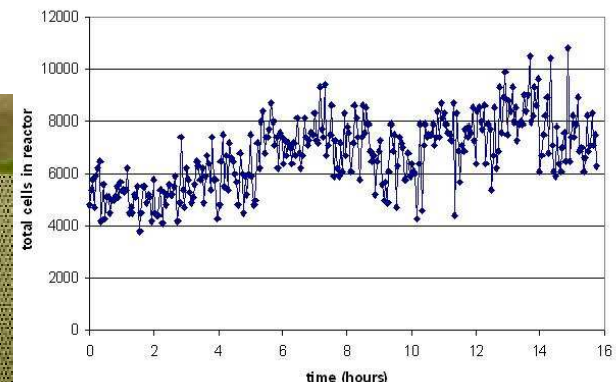
Lorenzo Sella
SH
(Mathematics, Leiden University)

Motivating examples

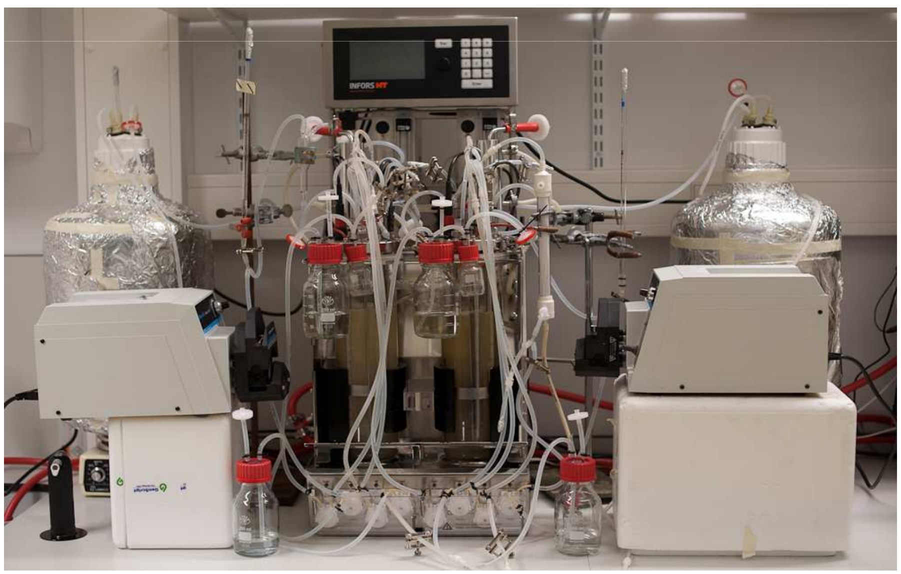
A.) Random interventions at fixed times

Sampling growing microbial colonies or (plant) cell suspension cultures

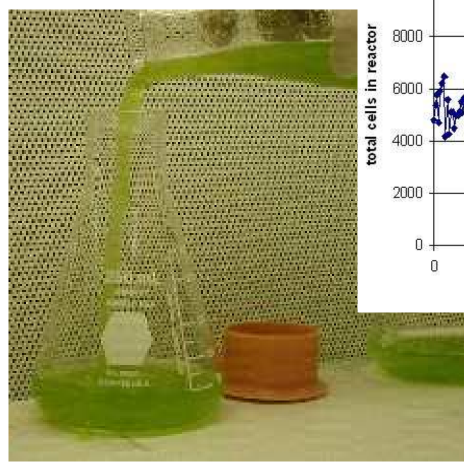
(as part of an experimental procedure)



Cell count (Bill Flanagan)



Fermentor (from Jeroen Siebring, Kuipers' Lab, RUG)



Cell suspension culture

Sample volume may be kept the same, variation in the number 'caught'

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Motivating examples

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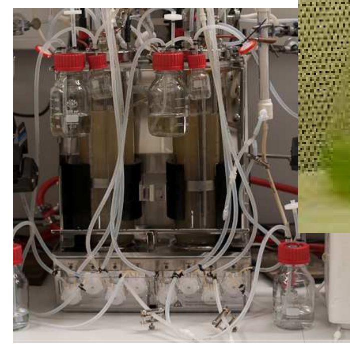
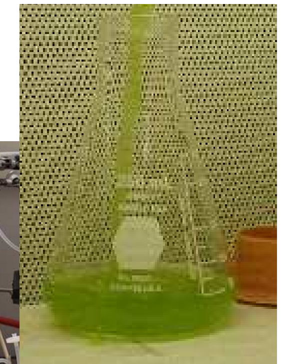
A.) Random interventions at fixed times

Sampling growing microbial colonies or (plant) cell suspension cultures





To what extent will sampling or harvesting influence the development of the bacterial / cell population?

Intuition:

Small samples will not matter too much.

But what is ‘small’ (and much)?

Applications
-- examples --

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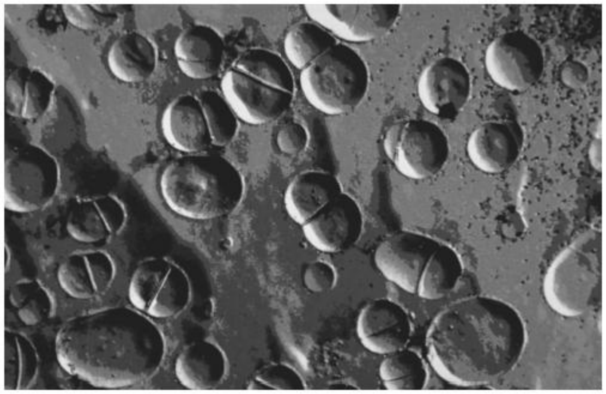
B.) Deterministic interventions at random times

A model for dividing cells
Lasota & Mackey
J. Math. Biol. **38** (1999), 241-261



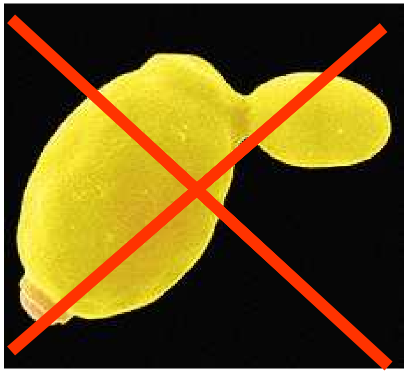
Dividing Streptococcus bacteria

Internal state of individual cell:

$$x(t) = (x_1(t), \ldots, x_d(t))$$

molecule numbers (not concentrations).

When cells divide, the molecules in the mother cell are distributed between mother and daughter cell



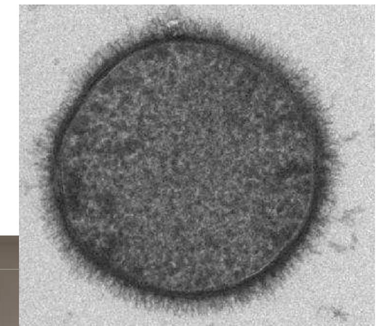
Budding yeast

Lasota & Mackey considered ***equal (deterministic) distribution*** at random division times

C.) Random interventions at random times

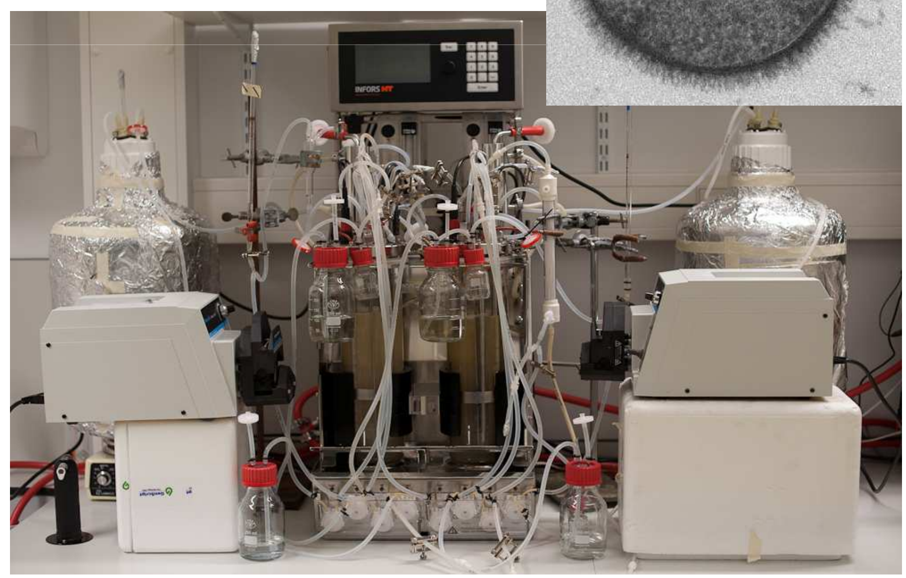
Growth in a random environment

Experimental microbiology group of Oscar Kuipers at Rijksuniversiteit Groningen (NL) grows *Bacillus subtilis* bacteria under varying conditions.



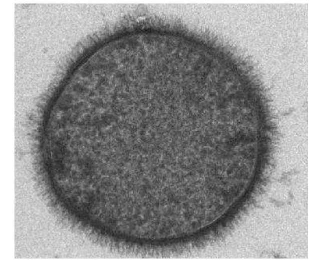
E.g. feeding glucose (a.o.) at randomly varying times intervals and/or in varying amounts

Bacillus subtilis (like other bacteria) has various survival strategies under resource limitations.



Fermentor (from Jeroen Siebring, Kuipers' Lab, RUG)

C.) Random interventions at random times



Growth in a random environment

Bacillus subtilis' survival strategies:

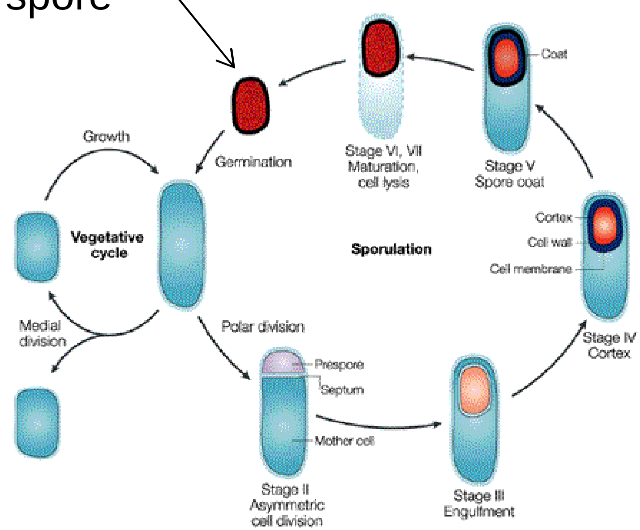
– activitation of **flagellar motility**,
to move towards new food sources

– secretion of **antibiotics**,
to feed on competing bacteria

– secretion of **hydrolytic enzymes**,
to scavenge extracelluar proteins

– induction of '**competence**',
feeding on and incorporating exogenous DNA

– **sporulation** (spore formation)

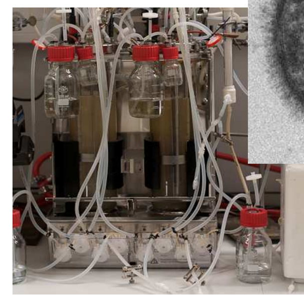


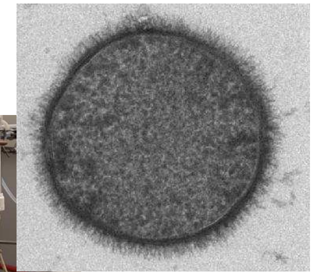
(Nature reviews: Microbiology)

Motivating examples

C.) Random interventions at random times

Growth in a random environment





It was observed in growth studies under resource limitations that:

- The ‘decision’ to sporulate is random: some cells do, others do not, under the same circumstances
- Under the same circumstances, the same effect for the population: fixed fraction of cells that have sporulated
- The fraction depends on the provided circumstances

For each ‘type of environment’ the population composition converges in simulations to a uniquely determined distribution.

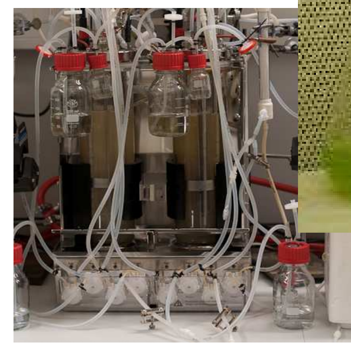
Can this be understood / proven analytically?

Part I

Mathematical modeling
and main mathematical question

A.) Random interventions at fixed times

Sampling / harvesting …



Simplest realistic model for population growth:

Verhulst's or ***logistic growth model***

Modification to the Malthusean exponential growth model

$$\frac{dv}{dt}(t) = rv(t)$$

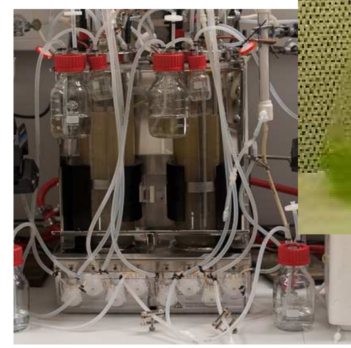
in which the growth rate r is limited by population size (e.g. due to a resource limitation)

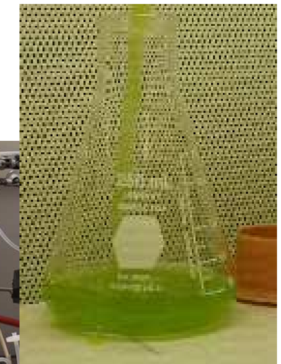
$$\frac{dv}{dt}(t) = r(1 - \frac{v(t)}{K})v(t)$$

Modeling
-- examples --

A.) Random interventions at fixed times

Sampling / harvesting …





Initial value problem:

$$\dot{v} = rv\left(1 - \frac{v}{K}\right), \qquad v(0) = v_0$$

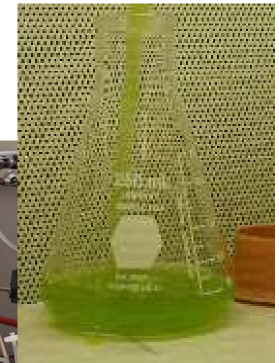
Unique solution for each $v_0 \in \mathbb{R}_+$: $\quad t \mapsto v(t; v_0)$

Solution operator: $\quad \phi_t : \mathbb{R}_+ \to \mathbb{R}_+ \qquad \phi_t(v_0) := v(t; v_0)$

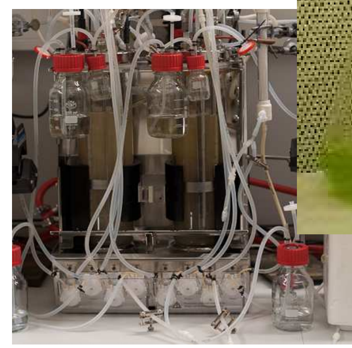
Explicit solution in this example:

$$v(t; v_0) = \left(\frac{1}{K} + \left(\frac{1}{v_0} - \frac{1}{K}\right)e^{-rt}\right)^{-1} \qquad (v_0 > 0)$$

A.) Random interventions at fixed times



Sampling / harvesting …



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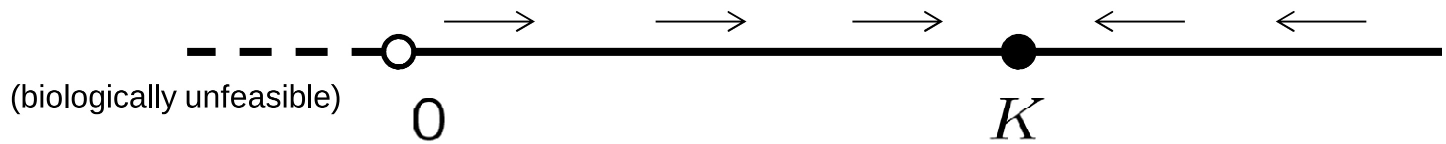
Solution operator: $\phi_t : \mathbb{R}_+ \to \mathbb{R}_+ \qquad \phi_t(v_0) := v(t; v_0)$

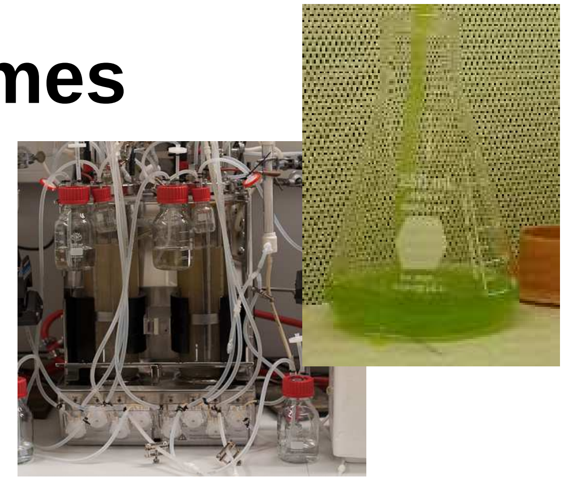
Explicit solution is not required:

Must understand the deterministic dynamics. Here simply



A.) Random interventions at fixed times

Sampling / harvesting …



Random size sample / catch:

There is a ***maximal catch size*** $m_c > 0$

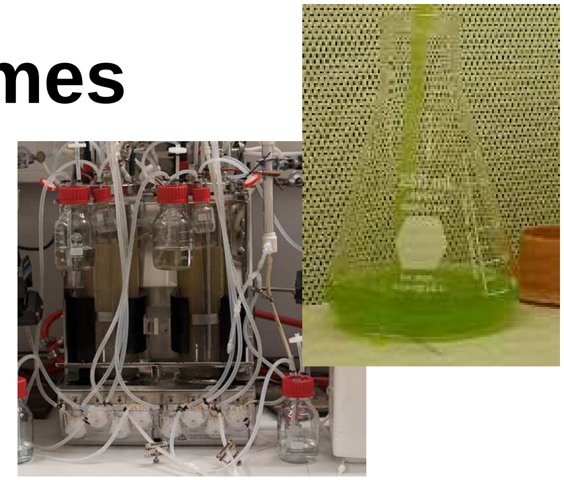
At time of intervention an instantaneous jump in population state $v \mapsto v'$ occurs, where the jump

$$Y = v' - v$$

has a distribution Q_v that depends on v:
the population size just before intervention.

A.) Random interventions at fixed times

Sampling / harvesting ...

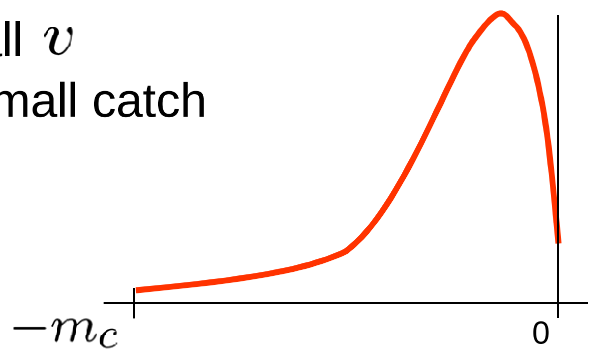


Random size sample / catch:

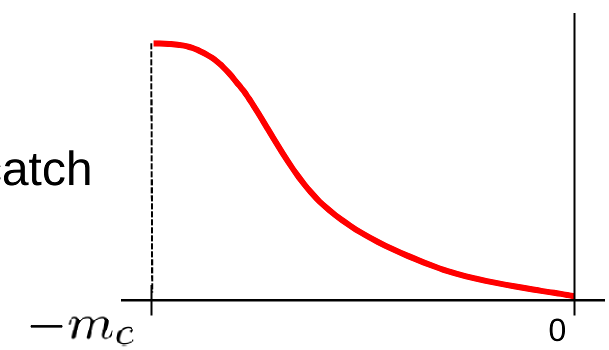
There is a ***maximal catch size*** $m_c > 0$

Y distribution (typical example):

small v
– small catch



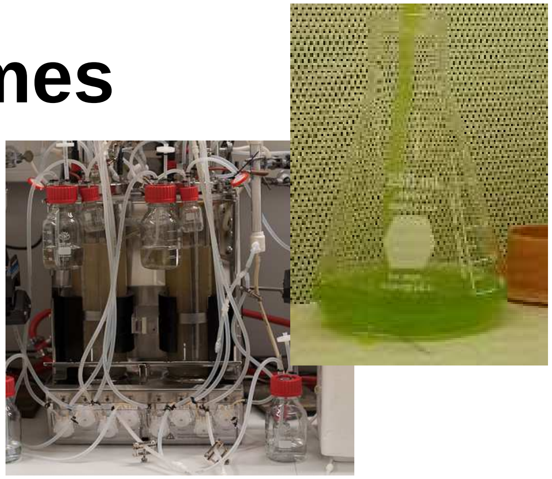
large v
– close to maximal catch



'State dependent jump distribution'

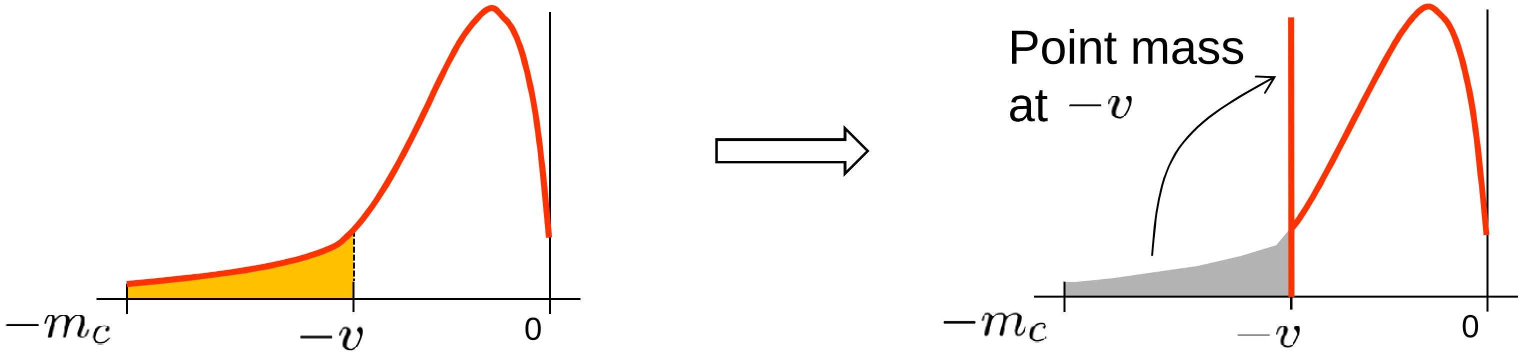
A.) Random interventions at fixed times

Sampling / harvesting …



For small v : one may catch all with positive probabilty, leading to population extinction.

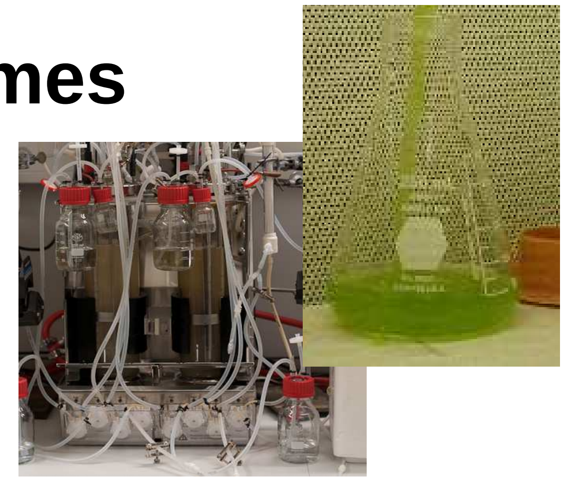
$$0 < v < m_c$$



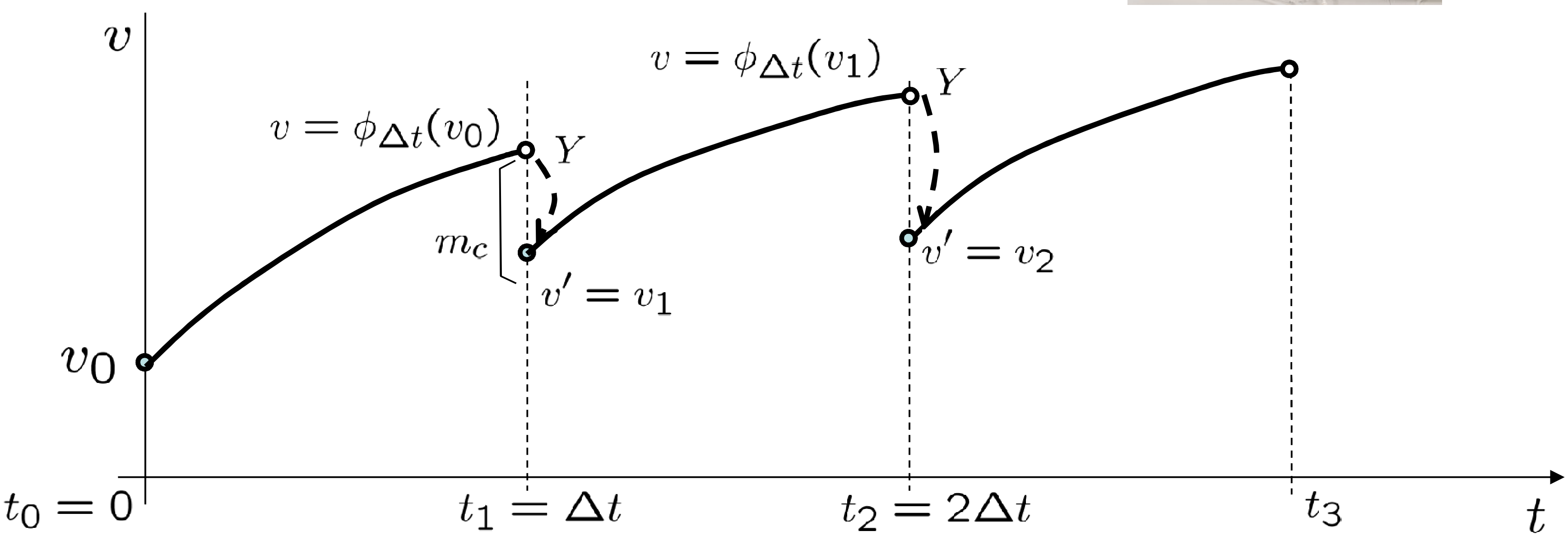
This assures that the state of the system remains in $\mathbb{R}_+$

Modeling
-- examples --

A.) Random interventions at fixed times
Sampling / harvesting …

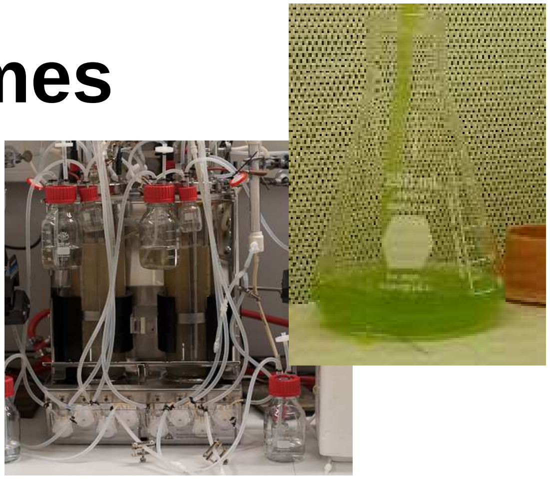


A realization of a trajectory:



A.) Random interventions at fixed times

Sampling / harvesting …



To analyze the long-term dynamics of the resulting process, consider

X_n : state of the system just after the n-th intervention, at $t = n\Delta t$

μ_n : distribution of X_n

Then

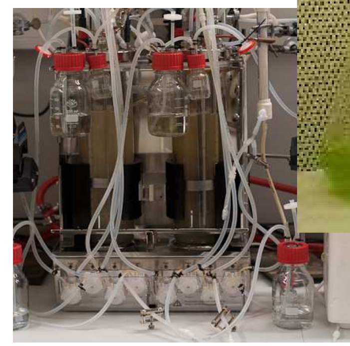
$$\mu_{n+1}(E) = \int_{\mathbb{R}_+} Q_v(E - v)\, d\mu'_n(v)$$

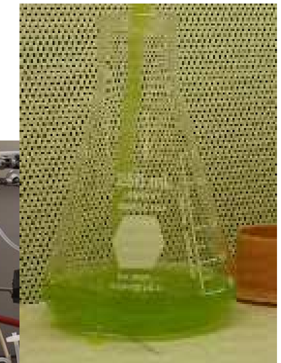
where $E \subset \mathbb{R}_+$,

μ'_n : distribution of the state just before n-th intervention

A.) Random interventions at fixed times

Sampling / harvesting …





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$$\mu_{n+1}(E) = \int_{\mathbb{R}_+} Q_v(E - v)\, d\mu_n'(v)$$

where $E \subset \mathbb{R}_+$,

$$\mu_n' := \phi_{\Delta t} \# \mu_n = \mu_n \circ \phi_{\Delta t}^{-1}$$

(push-forward)

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Modeling
-- examples --

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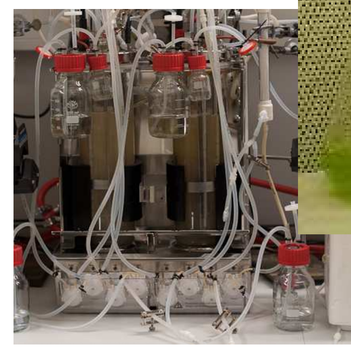
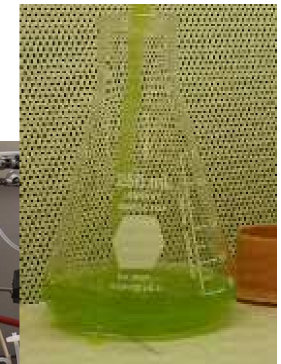
A.) Random interventions at fixed times

Sampling / harvesting …





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$$\mu_{n+1}(E) = \int_{\mathbb{R}_+} Q_{\phi_{\Delta t}(v)}(E - \phi_{\Delta t}(v))d\mu_n(v)$$

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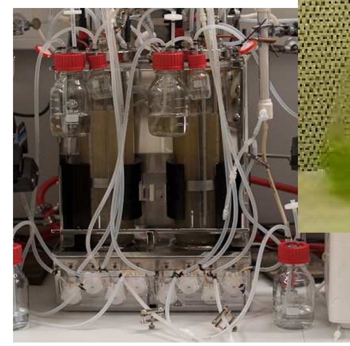
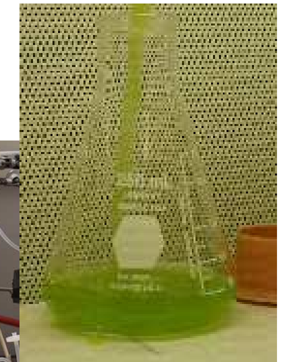
A.) Random interventions at fixed times





Sampling / harvesting …

To analyze the long-term dynamics of the resulting process, consider

P: operator on probability measures $\mathcal{P}(\mathbb{R}_+)$ on $\mathbb{R}_+$, defined by

$$P\mu(E) := \int_{\mathbb{R}_+} Q_{\phi_{\Delta t}(v)}(E - \phi_{\Delta t}(v))d\mu(v)$$

for $E \subset \mathbb{R}_+$ measurable.

Determine the possible dynamics of the associated map iteration:

$$P^n\mu, \qquad n \to \infty$$

Analysis frameworks

Determine the possible dynamics of $P^n\mu, \ n \to \infty$

1.) General theory of Markov chains

Meyn & Tweedie (1993 / 2009), Markov chains and stochastic stability

- T-chains, e-chains
- Applicable when state space is locally compact, Hausdorff.
- Focus on convergence to a unique invariant distribution

2.) Piecewise Deterministic Markov Processes (PDMPs)

Davis (1984), J.R. Statist. Soc. B **46** (3), 353-388.

Jacobsen (2006), Point process theory and applications

- Framework designed for varying intervention times
- Results not *readily* applicable to fixed time points
- Main results in locally compact state spaces (with few exceptions).

3.) **Stochastic Differential Equations** (SDEs)

– Current framework of SDEs does not fit…

$$dX = f(X_t)dt + g(X_t)dZ_t$$

Z_t : Brownian motion or jump process

Shape *of distribution of intervention must be allowed to depend on state, not 'only' amplitude…*

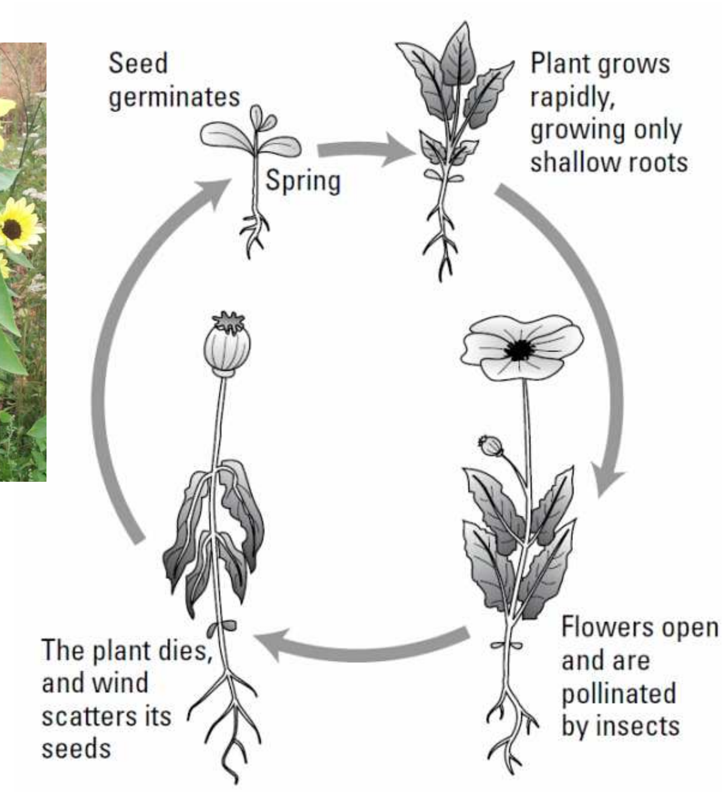
For particular applications, an approach that covers infinite dimensional state spaces is needed…

A.) Random interventions at fixed times

Population with non-overlapping generations

Many examples:

Annual plants



A.) Random interventions at fixed times

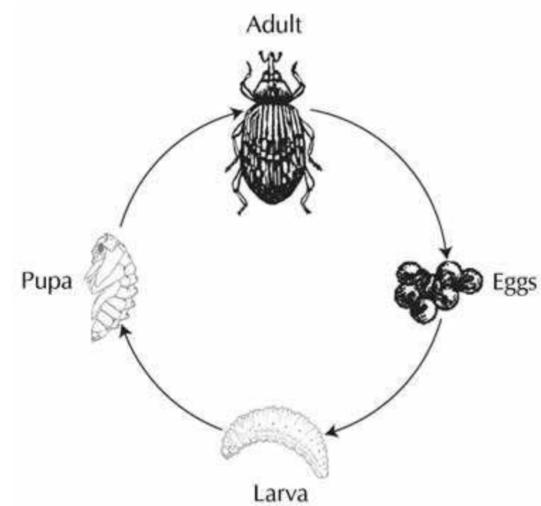
Population with non-overlapping generations

Many examples:

Annual plants

Insect populations

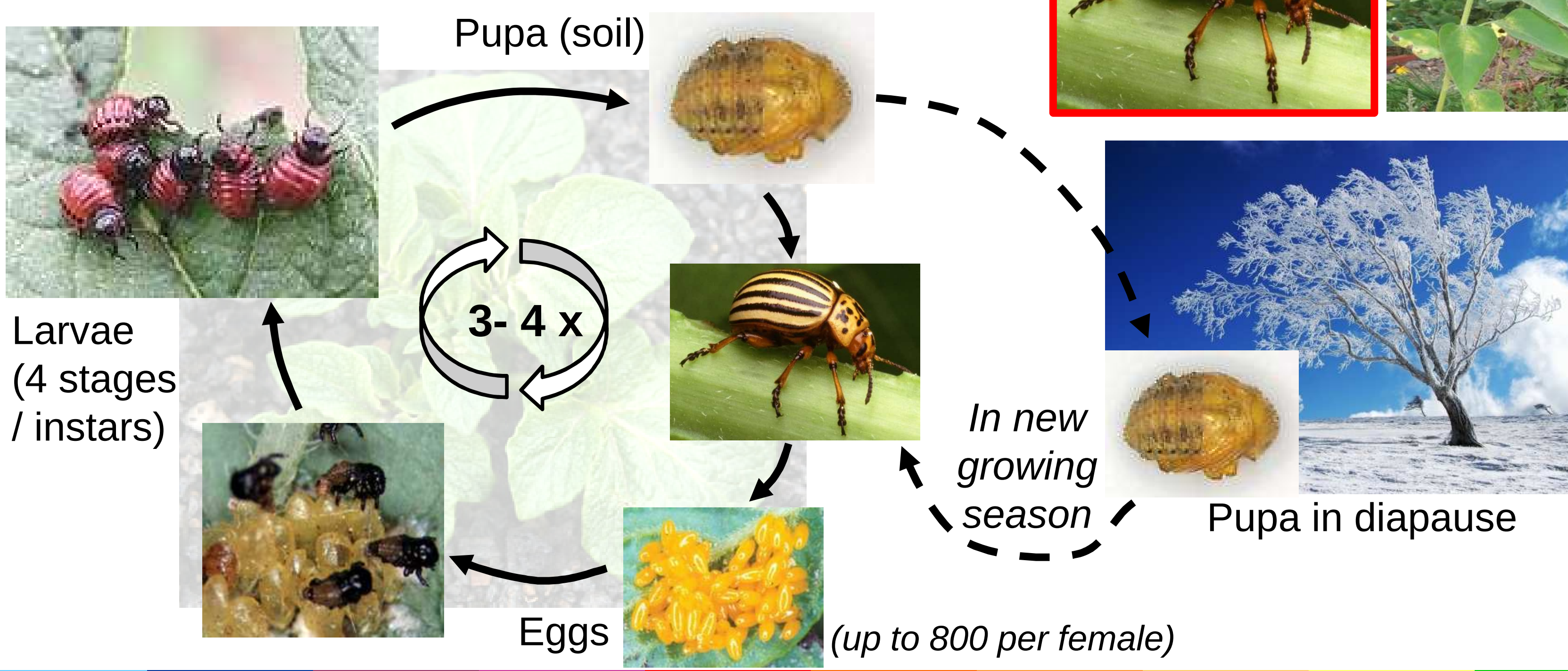
Pests: *potato beetle larvae*



A.) Random interventions at fixed times

Population with non-overlapping generations

Colorado potato beetle life cycle



Further applications
-- examples in infinite dimensions --

A.) Random interventions at fixed times

Population with non-overlapping generations

Questions:

How will the population of pest insect develop in the presence of natural predators?

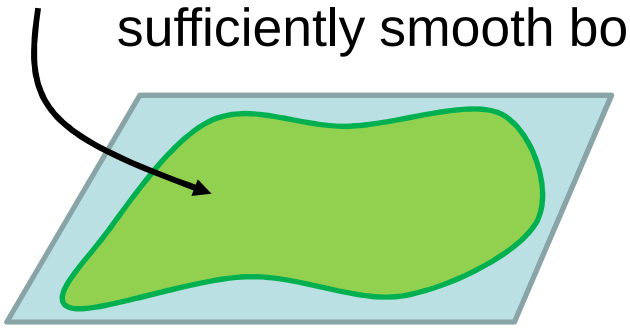
What are the effects of fluctuations in (long-term) weather conditions on population development?

A.) Random interventions at fixed times

Population with non-overlapping generations

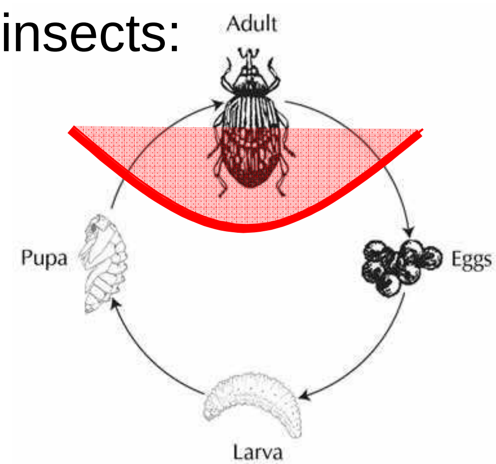
A population model:

Ω: bounded open subset of $\mathbb{R}^2$ with sufficiently smooth boundary $\partial\Omega$ (e.g. C^2)



'island' / 'region with natural impassable boundaries'

Two different species of insects:
prey – v ('victims')
predator – p



In ***dispersal stage*** each disperses over the domain, interacting with the other species, and reproducing.

Further applications
-- Infinite dimensions: a model --

A.) Random interventions at fixed times

Population with non-overlapping generations

A population model:

Dispersal and interaction:

$$\begin{cases} \partial_t v = D_v \Delta v + rv(1 - \frac{v}{K}) - a\frac{v}{b+v}p \\ \partial_t p = D_p \Delta p - dp + ah\frac{v}{b+v}p \end{cases}$$

(Neumann conditions on $\partial\Omega$)

Dispersal — Species reproduction and interaction during growth season

A.) Random interventions at fixed times

Population with non-overlapping generations

A population model:

Dispersal and interaction:

$$\begin{cases} \partial_t v = D_v \Delta v + rv(1 - \frac{v}{K}) - a\frac{v}{b+v}p \\ \partial_t p = D_p \Delta p - dp + ah\frac{v}{b+v}p \end{cases}$$

(Neumann conditions on $\partial\Omega$)

(for $0 \leq t \leq t_e$; t_e : duration of growth season)

Pupae in diapause for each species:

$$w(x,t) = \int_0^t R_v(s, v(x,s))ds \qquad q(x,t) = \int_0^t R_p(s, p(x,s))ds$$

Further applications
-- Infinite dimensions: a model --

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A.) Random interventions at fixed times

Population with non-overlapping generations

A population model:

A fraction of the pupae in diapause at a location will re-emerge as adult in the next growing season.

Survival from diapause:
the initial conditions v_0' and p_0' for the next generation dispersal stage

$$v_0' = S_v(w(t_e)) \qquad p_0' = S_p(q(t_e))$$

Further applications
-- Infinite dimensions: a model --

A.) Random interventions at fixed times

Population with non-overlapping generations

A population model:

Thus, we obtain a deterministic map

$$\phi : C(\overline{\Omega})^2 \to C(\overline{\Omega})^2$$

that maps the population composition at the start of the growth season to the corresponding situation at start of the next:

$$\partial_t v = D_v \Delta v + rv(1 - \frac{v}{K}) - a\frac{v}{b+v}p$$
$$\partial_t p = D_p \Delta p - dp + ah\frac{v}{b+v}p$$

$$w(x,t) = \int_0^t R_v(s, v(x,s))ds$$
$$q(x,t) = \int_0^t R_p(s, p(x,s))ds$$

$$v_0' = S_v(w(t_e))$$
$$p_0' = S_v(q(t_c))$$

$$(v_0, p_0) \longrightarrow (v,p) \longrightarrow (w,q) \longrightarrow (v_0', p_0')$$

$$\phi : (v_0, p_0) \mapsto (v_0', p_0')$$

Further applications
-- Infinite dimensions: a model --

A.) Random interventions at fixed times

Population with non-overlapping generations

A population model:

Addition of randomness in:

survival from diapause
- predation during winter
- harshness of winter

duration of growth season
- weather conditions

(population (sub)model for the growing season)

Further applications
-- Infinite dimensions: a model --

A.) Random interventions at fixed times

Population with non-overlapping generations

Model distribution of the state of the system at the start of each growing season (year)

Similar set-up as for the logistic growth model, but now in infinite dimensional state space

The fixed-time problem
-- general formulation --

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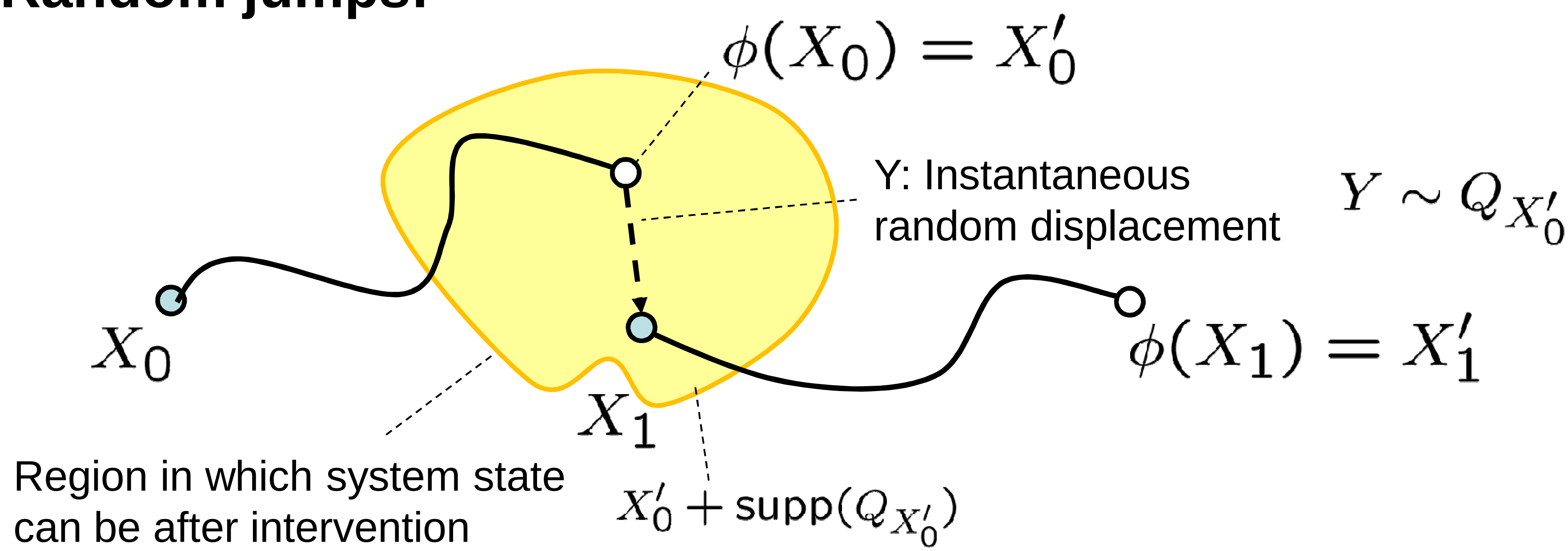
Deterministic system:

X: (separable) Banach space

$S \subset X$: closed subset

$\phi : S \to S$: continuous map (e.g. given by a solution operator $\phi = \phi_{\Delta t}$)

Random jumps:



The fixed-time problem
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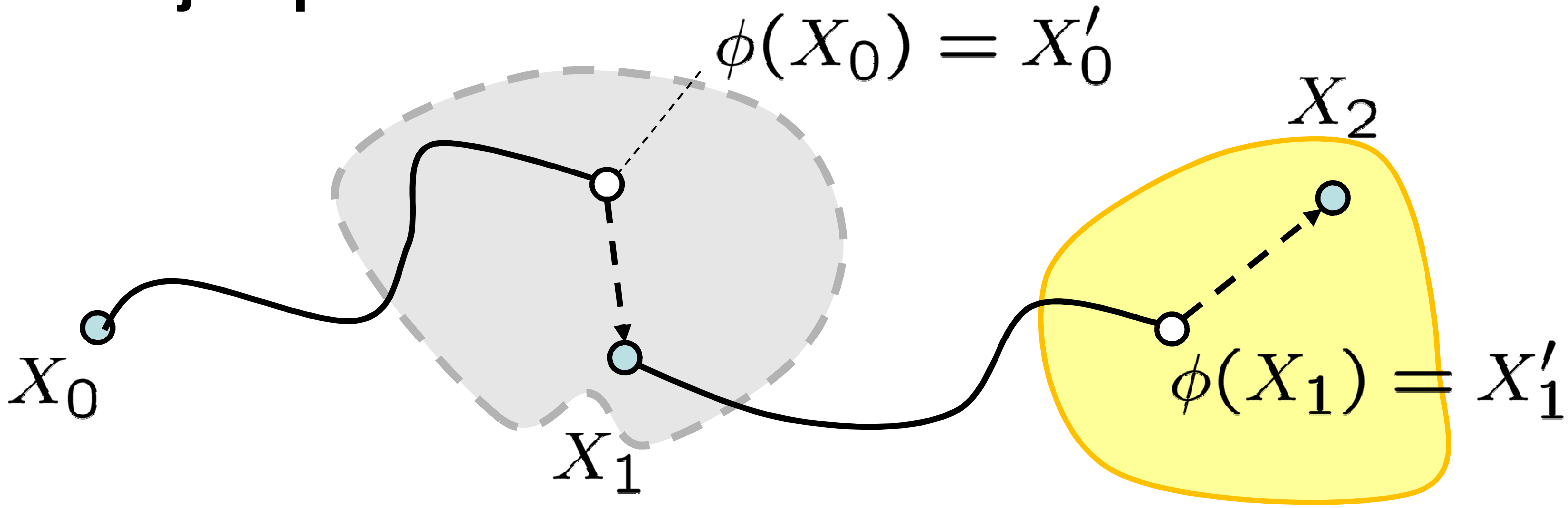

The fixed-time problem
-- general formulation --

Deterministic system:

X: (separable) Banach space

$S \subset X$: closed subset

$\phi : S \to S$: continuous map (e.g. given by a solution operator $\phi = \phi_{\Delta t}$)

Random jumps:

$Y_n = X_n - X'_{n-1} \sim Q_{X'_{n-1}}$

+ condition on $\mathrm{supp}(Q_x)$ such that $X_n \in S$ for all n

The states $X_0, X_1, X_2, \ldots$ form a Markov chain
with transition operator:

$$P\mu(E) = \int_\Omega Q_{\phi(x)}(E - \phi(x))d\mu(x)$$

Determine the possible dynamics of $P^n\mu,\ n\to\infty$

Analysis frameworks
-- applicability in infinite dimensions --

Determine the possible dynamics of $P^n\mu,\ n \to \infty$

1.) General theory of Markov chains

Meyn & Tweedie (1993 / 2009), Markov chains and stochastic stability

- T-chains, e-chains
- Applicable when state space is locally compact, Hausdorff.
- Focusses on convergence to a unique invariant distribution

2.) Piecewise Deterministic Markov Processes (PDMPs)

Davis (1984), J.R. Statist. Soc. B **46** (3), 353-388.

Jacobsen (2006), Point process theory and applications

- Framework designed for varying intervention times
- Results not *readily* applicable to fixed time points
- Main results in locally compact state spaces (with few exceptions).

What does work in non-locally compact state spaces?

4.) Theory for Markov operators that satisfy particular *equicontinuity properties*

- **non-expansive Markov operators**
- **e-property** (in different variants)

-- Break --

Part II

Mathematical preliminaries

Mathematical preliminaries

Recall main (mathematical) question:

Determine the possible dynamics of $P^n\mu,\ \ n \to \infty$

So we need to discuss:

(1) Useful topologies on spaces of measures ($\mathcal{M}(S)$, $\mathcal{M}^+(S)$,$\mathcal{P}(S)$, ...)

(2) Regularity classes for P, relative to these topologies

Mathematical preliminaries
-- notation --

Assume throughout that S is a Polish space,
d a metric on S that metrizes the topology, yielding a complete separable metric space

View S as a measurable space, with its Borel σ-algebra Σ .

$\mathcal{M}(S)$: finite (signed) measures on S
$\mathcal{M}^+(S)$: finite positive measures on S
$\mathcal{P}(S)$: probability measures on S

δ_x: Dirac (point) measure at x

$$\delta_x(E) = \begin{cases} 1, & \text{if } x \in E \\ 0, & \text{otherwise} \end{cases}$$

$BM(S)$: bounded measurable functions
$C_b(S)$: bounded continuous functions

$$\|f\|_\infty := \sup_{x \in S} |f(x)|$$

Various definitions circulate:

1.) On measures:

Definition: a ***Markov operator*** on S is a map $P : \mathcal{M}^+(S) \to \mathcal{M}^+(S)$
that satisfies: $P(a\mu + \nu) = aP(\mu) + P(\nu) \quad (a \geq 0)$

$$P\mu(S) = \mu(S)$$

2.) On densities: replace $\mathcal{M}^+(S)$ by an L^1-space: $L^1(S, \mu_0)$

3.) Dually, on functions:

A (dual) *Markov operator* on S is a map $U : BM(S) \to BM(S)$
that is linear, positive and satisfies: $U\mathbf{1} = \mathbf{1}$

$BM(S)$: bounded measurable functions

Total variation norm: the natural metric related to ordering

$\mathcal{M}(S)$ is an ***ordered vector space***:

$$\mu \leq \nu \quad \text{iff} \quad \mu(E) \leq \nu(E) \quad \text{for all } E \in \Sigma$$

$(\mathcal{M}(S), \leq)$ has a ***lattice structure***:

$$\mu \wedge \nu(E) = \inf\{\mu(A) + \nu(E \setminus A) : A \in \Sigma,\ A \subset E\}$$

$$\mu \vee \nu(E) = \sup\{\mu(A) + \nu(E \setminus A) : A \in \Sigma,\ A \subset E\}$$

The ***Jordan decomposition*** derives from these:

$$\mu^+ := \mu \vee 0 \qquad \mu^- := (-\mu)^+ = -(\mu \wedge 0)$$

$$\mu = \mu^+ - \mu^-$$

Total variation norm: the natural metric related to ordering

$$\mu = \mu^+ - \mu^- \qquad\qquad |\mu| := \mu^+ + \mu^-$$

$(\mathcal{M}(S), \leq)$ is a ***Banach lattice***:

There exists an unique norm (up to equivalence) $\|\cdot\|$ on $\mathcal{M}(S)$ such that the lattice operations ($\vee$, $\wedge$) are continuous and

$$\|\mu\| = \|\,|\mu|\,\| \quad \text{for all} \quad \mu \in \mathcal{M}(S)$$

Total variation norm: $\|\mu\|_{TV} := |\mu|(S)$

$$\|\mu\|_{TV} := \sup_{E\in\Sigma} \mu(E) - \inf_{E\in\Sigma} \mu(E)$$

(This holds for any measurable space (S,Σ))

Total variation norm: the natural metric related to ordering

If S is a topological space, Σ its Borel σ-algebra, then

$$\|\mu\|_{TV} = \sup\{|\int f d\mu| : f \in C_b(S), \|f\| \leq 1\}$$

That is, $\mathcal{M}(S)$ is viewed as linear subspace of the dual $C_b(S)^*$ of $C_b(S)$, equipped with the restriction of the dual norm.

The maps $\mu \mapsto \mu^{\pm}$ are continuous, but generally $x \mapsto \delta_x$ is **not**

$$\|\delta_x - \delta_y\|_{TV} := 2 \quad \text{if} \quad x \neq y$$

The latter can be 'repaired' by using the weak topology $\sigma(\mathcal{M}(S), C_b(S))$
Continuity of lattice operations is then lost.

Fortet-Mourier or Dudley norm

S a Polish space; d: metric such that (S,d) is separable and complete

$BL(S)$: space of bounded Lipschitz functions (for d):
all $f \in C_b(S)$ for which

$$|f|_{Lip,d} := \sup\left\{ \frac{|f(x) - f(y)|}{d(x,y)} \;:\; x,y \in S,\; x \neq y \right\} < \infty$$

Two equivalent norms on $BL(S)$ that make it a Banach space:

$$\|f\|_{BL} := \|f\|_\infty + |f|_{Lip,d} \qquad \textit{(Dudley)}$$

$$\|f\|_{FM} := \max(\|f\|_\infty, |f|_{Lip,d}) \qquad \textit{(Fortet-Mourier)}$$

$$\|f\|_{FM} \;\leq\; \|f\|_{BL} \;\leq 2\|f\|_{FM}$$

Fortet-Mourier or Dudley norm

Lemma: (Dudley 1966)

$$\mathcal{M}(S) \to BL^*(S) : \mu \mapsto \phi_\mu(f) := \int f d\mu$$ is injective.

$\mathcal{M}(S)_{BL}$: space of measures equipped with dual norm of $BL^*(S)$ for Dudley norm;

$$\|\mu\|_{BL}^* = \sup\{|\int f d\mu| : f \in BL(S), \|f\|_{BL} \leq 1\}$$

Similarly,

$\mathcal{M}(S)_{FM}$: space of measures equipped with dual norm of $BL^*(S)$ for Fortet-Mourier norm;

$$\|\mu\|_{FM}^* = \sup\{|\int f d\mu| : f \in BL(S), \|f\|_{FM} \leq 1\}$$

Mathematical preliminaries
-- (metric) topologies on measures --

$(\mathcal{M}(S), \|\cdot\|_{BL}^*)$ is **not complete generally**

The map $x \mapsto \delta_x$ is continuous, but generally $\mu \mapsto \mu^{\pm}$ are **not**

For $\mu \in \mathcal{M}^+(S)$ one has: $\|\mu\|_{TV} = \|\mu\|_{BL}$

Some interesting functional analytic properties:

Theorem: (Dudley, 1966)
The restriction of the $\sigma(\mathcal{M}(S), C_b(S))$ weak topology to $\mathcal{M}^+(S)$ equals the restriction of the $\|\cdot\|_{BL}^*$ -norm topology.

Theorem: (H. & Worm, 2009)

$$\mathcal{M}(S)_{BL}^* \simeq BL(S)$$

Back to the main mathematical question:

Determine the possible dynamics of $P^n\mu, \;\; n \to \infty$

Simplest possible behaviour:

Definition: a Markov operator P on S is ***asymptotically stable*** with respect to the norm $\|\cdot\|$ on $\mathcal{M}(S)$ when it has a unique invariant measure μ^* , i.e. $P\mu^* = \mu^*$ such that for all $\mu \in \mathcal{P}(S)$.

$$\|P^n\mu - \mu^*\| \to 0$$

('*Everything converges to* μ^* ')

Mathematical preliminaries
-- regularity of Markov operators --

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Definition: a Markov operator P on S is ***regular*** when there is a dual Markov operator U such that $\langle P\mu, f\rangle = \langle \mu, Uf\rangle$ for all $f \in BM(S)$.

Definition: a regular Markov operator P on S is ***Feller*** when the dual operator U satisfies $U(C_b(S)) \subset C_b(S)$.

Equivalent non-dual formulation:

P is continuous for the $\|\cdot\|_{BL}^{*}$ - norm topology

$x \mapsto P\delta_x : S \to \mathcal{M}(S)$ is continuous for the $\|\cdot\|_{BL}^{*}$ - norm

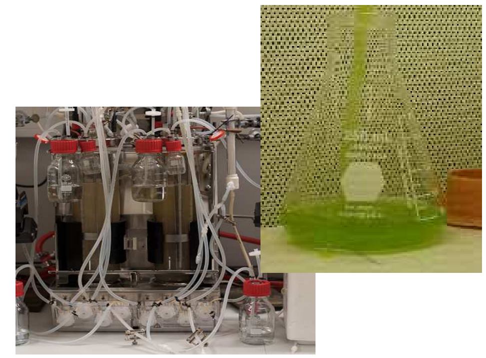
Definition: a Markov operator P on S is ***ultra-Feller*** when $x \mapsto P\delta_x : S \to \mathcal{M}(S)$ is continuous for the $\|\cdot\|_{TV}$ - norm topology

Ultra-Feller $\overset{\not\Leftarrow}{\Longrightarrow}$ **Feller** $\overset{\not\Leftarrow}{\Longrightarrow}$ **Regular**

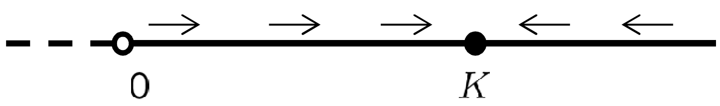
Part II

Approach to mathematical analysis

Recall the mathematical set-up:

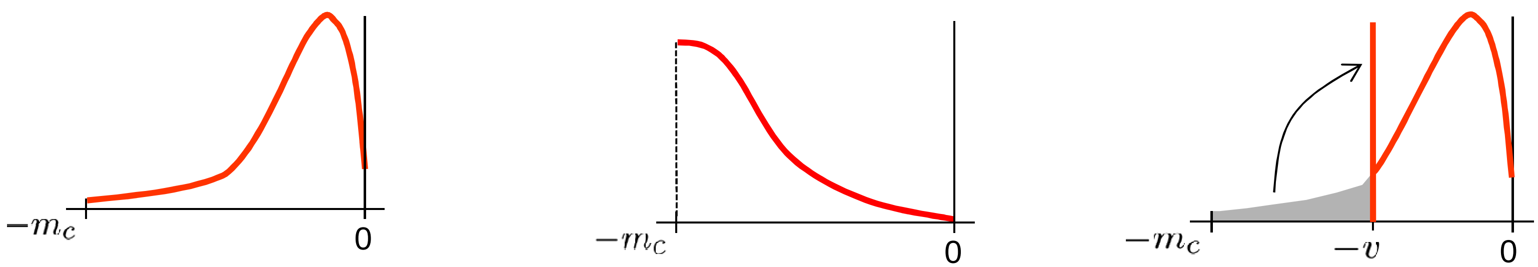


$$\dot{v}(t) = rv(1 - \frac{v}{K})$$



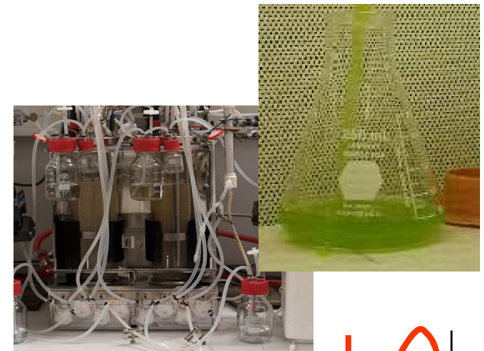
$$\phi_t(v_0) := v(t; v_0)$$ *(deterministic system)*

$$Q_v: \quad \mathrm{supp}(Q_v) = [\max(-m_c, -v), 0]$$ *(distribution for random jumps)*

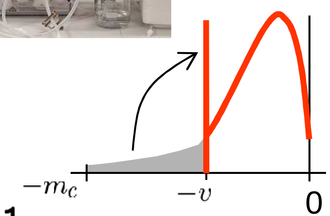


$$P\mu(E) := \int_{\mathbb{R}_+} Q_{\phi_{\Delta t}(v)}(E - \phi_{\Delta t}(v))d\mu(v)$$ *(Markov operator)*

Establish particular regularity of P



$$P\mu(E) := \int_{\mathbb{R}_+} Q_{\phi_{\Delta t}(v)}(E - \phi_{\Delta t}(v))\,d\mu(v)$$



(A1) $\mathrm{supp}(Q_v) = [\max(-m_c, -v), 0]$ for all $v > 0$;

(A2) $Q_v = e_v \delta_{-v} + q_v d\lambda$, with $e_v = 0$ when $v \geq m_c$

(A3) $v \mapsto (e_v, q_v)$ is continuous as map $(0,\infty) \to [0,1] \times L^1(\mathbb{R}_+)$

(A4) $Q_v((-v, 0]) \to 0$ as $v \downarrow 0$.

(the fewer individuals there are, the more likely you catch them all.)

Theorem: (A1) – (A4) imply that P is ultra-Feller on $\mathbb{R}_+$.

(i.e., $x \mapsto P\delta_x : S \to \mathcal{M}(S)_{TV}$ is continuous)

The sampling problem
-- an analysis approach --

How to approach the problem of asymptotic stability?

1. '***Trace supports***'

Obtaining information on the support of the invariant measure is interesting in itself, because the computation of the precise distribution will often be (too) hard to achieve.

(A1) $\mathrm{supp}(Q_v) = [\max(-m_c, -v), 0]$ for all $v > 0$;

yields

$$\mathrm{supp}(P\delta_x) = [(\phi_{\Delta t}(x) - m_c)^+, \phi_{\Delta t}(x)]$$

How to approach the problem of asymptotic stability?

1. ‘***Trace supports***’

So define

$$\psi(x) := [\phi_{\Delta t}(x) - m_c]^+$$

Then

$$\mathsf{supp}(P^n\delta_x) = [\psi^n(x), \phi_{n\Delta t}(x)]$$

Dynamics of iterating ψ :

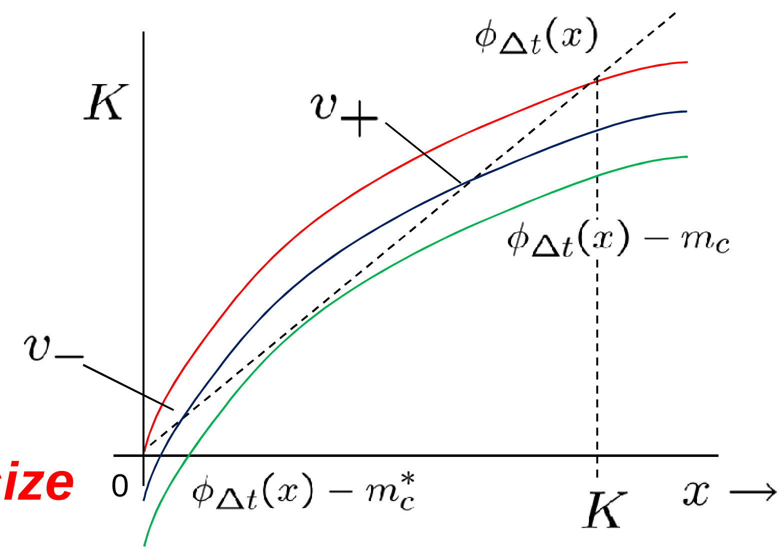
Two fixed points:

$\psi(x) = x$ iff $x = v_\pm$

If $m_c > m_c^*$, no fixed points

$$m_c^* := K\frac{e^{r\Delta t/2} - 1}{e^{r\Delta t/2} + 1}$$

critical catch size



How to approach the problem of asymptotic stability?

1. ‘***Trace supports***’

So define

$$\psi(x) := [\phi_{\Delta t}(x) - m_c]^+$$

Then

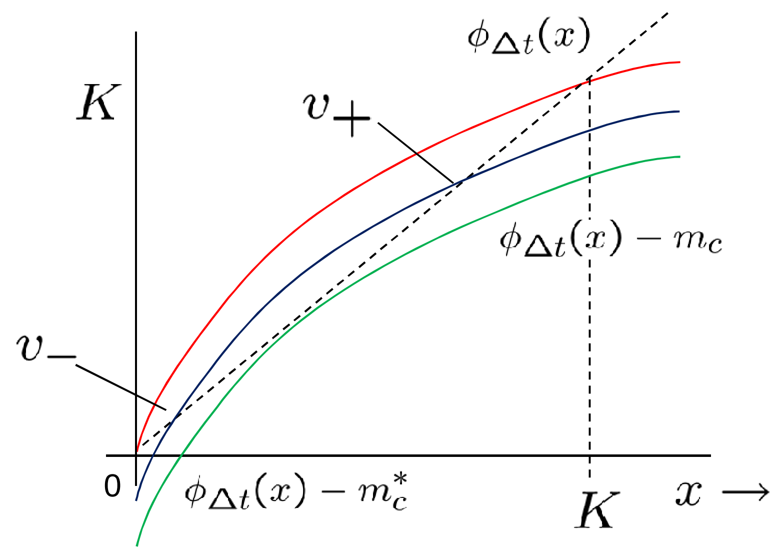
$$\mathrm{supp}(P^n \delta_x) = [\psi^n(x), \phi_{n\Delta t}(x)]$$

Dynamics of iterating ψ :

If $0 < m_c < m_c^* < K$:

$$\psi^n(x) \to v_+ \text{ if } x > v_-$$

$$\psi^n(x) \to 0 \text{ if } x < v_-$$



How to approach the problem of asymptotic stability?

1. ‘*Trace supports*’
2. **Use general result:**

Theorem: (In this formulation: Alkurdi, H. & Van Gaans, 2013)

Let P be a regular Markov operator on a Polish space such that there exists $N \in \mathbb{N}$ for which

$$\alpha := \inf_{x,y \in S} \|P^N \delta_x \wedge P^N \delta_y\|_{TV} > 0$$

Then for all $n \geq N$ one has for all $\mu, \nu \in \mathcal{P}(S)$

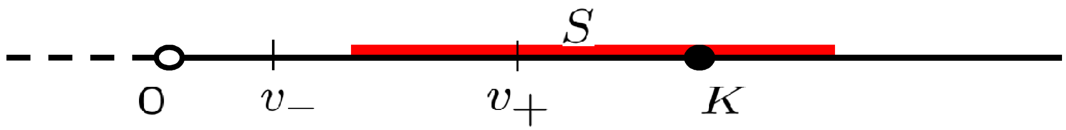
$$\|P^n(\mu - \nu)\|_{TV} \leq \theta^n \|\mu - \nu\|_{TV}$$

Where $\theta = (1 - \alpha)^{1/N} < 1$.

The sampling problem
-- an analysis approach --

How to verify $\alpha := \inf_{x,y \in S} \|P^N\delta_x \wedge P^N\delta_y\|_{TV} > 0$?

(where $S = [r, R]$ with $v_- \le r \le v_+$, $R \ge K$ in this case)

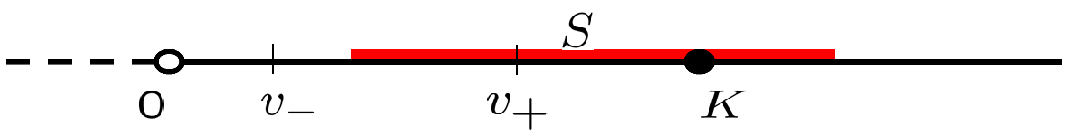


(S is invariant under P)

The sampling problem
-- an analysis approach --

How to verify $\alpha := \inf_{x,y\in S} \|P^N\delta_x \wedge P^N\delta_y\|_{TV} > 0$?

(where $S = [r, R]$ with $v_- \leq r \leq v_+$, $R \geq K$ in this case)



Use obtained information on the dynamics of supports:

$$\text{supp}(P^n\delta_x) = [\psi^n(x), \phi_{n\Delta t}(x)]$$

$$\psi^n(x) \to v_+ \text{ if } x > v_- \qquad \psi(v_-) = v_- \qquad \phi_{n\Delta t}(x) \to K \text{ if } x > 0$$

1. There exists N such that for all $x, y \in S$

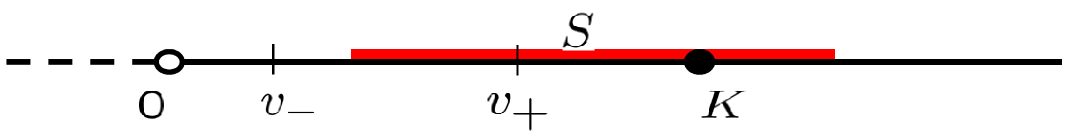
$$(\psi^N(x), \phi_{N\Delta t}(x)) \cap (\psi^N(y), \phi_{N\Delta t}(y)) \neq \emptyset$$

(use compactness of S here, a.o.…)

The sampling problem
-- an analysis approach --

How to verify $\alpha := \inf_{x,y \in S} \|P^N \delta_x \wedge P^N \delta_y\|_{TV} > 0$?

(where $S = [r, R]$ with $v_- \leq r \leq v_+$, $R \geq K$ in this case)



1. There exists N such that for all $x, y \in S$

$$(\psi^N(x), \phi_{N\Delta t}(x)) \;\cap\; (\psi^N(y), \phi_{N\Delta t}(y)) \neq \emptyset$$

2. Therefore, $P^N \delta_x \wedge P^N \delta_y \neq 0$ for all $x, y \in S$

($\mu \wedge \nu(E) = \inf\{\mu(A) + \nu(E \setminus A) : A \in \Sigma,\ A \subset E\}$)

The sampling problem
-- an analysis approach --

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How to verify $\alpha := \inf_{x,y\in S} \|P^N\delta_x \wedge P^N\delta_y\|_{TV} > 0$?

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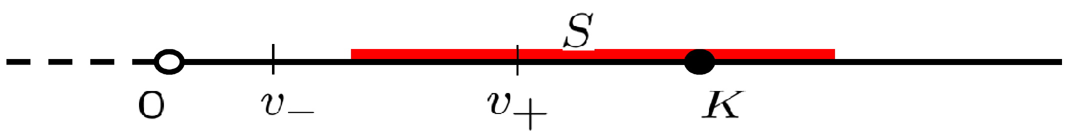

1. There exists N such that for all $x, y \in S$

$$(\psi^N(x), \phi_{N\Delta t}(x)) \;\cap\; (\psi^N(y), \phi_{N\Delta t}(y)) \neq \emptyset$$

2. Therefore, $P^N\delta_x \wedge P^N\delta_y \neq 0$ for all $x, y \in S$

$x \mapsto P^N\delta_x : S \to \mathcal{M}(S)_{TV}$ is continuous *(ultra-Feller property)*, so

3. $(x, y) \mapsto \|P^N\delta_x \wedge P^N\delta_y\|_{TV}$ is continuous.

4. The bound for α away from 0 now follows from compactness of S

The sampling problem
-- an analysis approach --

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Theorem: (Alkurdi, H. & Van Gaans 2013)

Let $0 < m_c < m_c^* < K$. The interval $[v_-,\infty)$ is P-invariant and the restriction has a unique invariant measure μ^* with support $[v_+,K]$

For any measure μ for which $\mathrm{supp}(\mu) \subset [v_-,\infty)$,

$$\|P^n\mu - \mu^*\|_{TV} \to 0$$

That is, μ^* is asymptotically stable on $[v_-,\infty)$.

Moreover, the rate of convergence is exponential for measures with compact support.

$m_c^* := K\dfrac{e^{r\Delta t/2}-1}{e^{r\Delta t/2}+1}$ *(critical catch size)* ⟷ How large can be '*small interventions*'

Support of μ^* is $[v_+,K]$ ⟷ How much effect?

The sampling problem
-- an analysis approach --

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This is not all behaviour of $P^n\mu,\ n \to \infty$, in this case

δ_0 is another invariant measure of P

$$P\delta_0(E) := Q_{\phi_{\Delta t}(0)}(E - \phi_{\Delta t}(0)) = Q_0(E)$$
$$= \delta_0(E)$$

Because, according to (A1),

$$\mathrm{supp}(Q_0) = [\max(-m_c, 0), 0] = \{0\}$$

Theorem: (Alkurdi, H., Van Gaans, 2013)

δ_0 and μ^* are *all* ergodic measures for P on $\mathbb{R}_+$. Thus, any invariant measure is a convex combination of these two ergodic measures.

The sampling problem
-- an analysis approach --

This is not all behaviour of $P^n\mu,\ n\to\infty$, in this case

Define the Cesaro-averages:

$$P^{(n)}\mu := \frac{1}{n}\sum_{k=0}^{n-1} P^k\mu$$

For any $x\geq 0$, $P^{(n)}\delta_x$ converges to an invariant measure (for $\|\cdot\|_{FM}^*$).
Hence,

$$\lim_{n\to\infty} P^{(n)}\delta_x = p(x)\delta_0 + (1-p(x))\mu^*$$

$p(x)$ may be interpreted as the '**extinction probability**', because of

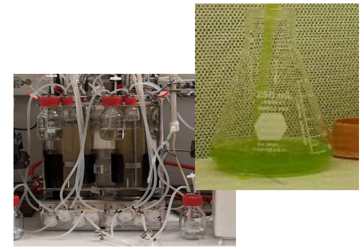
Theorem: (Alkurdi, H., Van Gaans, 2013)

$$\lim_{n\to\infty} P^n\delta_x(\{0\}) = p(x) \qquad \lim_{n\to\infty} P^n\delta_x([v_-,\infty)) = 1-p(x)$$

One can show that $p(x)$ is continuous.

The sampling problem
-- an analysis approach --

Summary of approach



1. Study the dynamics of supports $\text{supp}(P^n \delta_x)$ as $n \to \infty$

2. Use (1), **compactness** of S, and **ultra-Feller property** of P to obtain a lower-bound type of estimate:

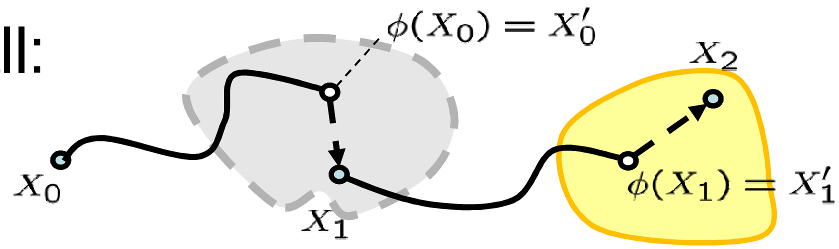
$$\alpha := \inf_{x,y \in S} \|P^N \delta_x \wedge P^N \delta_y\|_{TV} > 0$$

3. Apply general result yielding exponential rate convergence in $\|\cdot\|_{TV}$

How to approach the infinite dimensional case?

In infinite dimensions
-- sketch --

Recall:



X: (separable) Banach space

$S \subset X$: closed subset

$\phi : S \to S$: continuous map $\quad P\mu(E) = \int_\Omega Q_{\phi(x)}(E - \phi(x))d\mu(x)$

Focus on **persistence of asymptotic stability** of equilibria of ϕ :

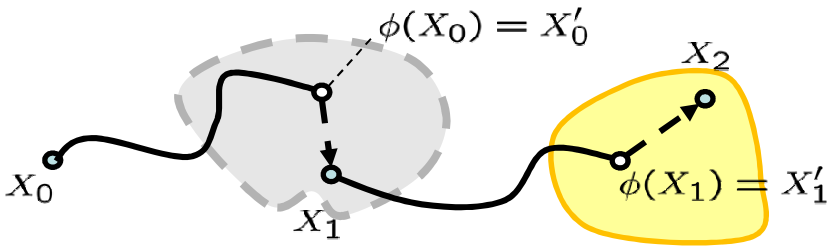
$\phi(x^*) = x^*$

(A1') ϕ is a strict contraction on a closed ball B^* around x^*

(A2') $\phi : B^* \to B^*$ is a compact map

(replaces the compactness of state space; holds for diffusion in e.g $C(\overline{\Omega})$ *)*

In infinite dimensions
-- sketch --



$$P\mu(E) = \int_\Omega Q_{\phi(x)}(E - \phi(x))d\mu(x)$$

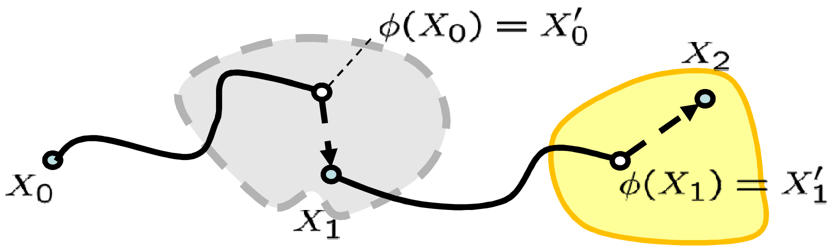
(A1') ϕ is a strict contraction on a closed ball B^* around x^*

(A2') $\phi : B^* \to B^*$ is a compact map

(A3') $\|Q_x - Q_y\|_{FM} \leq L\|x - y\|$

(replaces (A3) $v \mapsto (e_v, q_v)$ is continuous as $(0, \infty) \to [0, 1] \times L^1(\mathbb{R}_+)$

In infinite dimensions
-- sketch --



$$P\mu(E) = \int_\Omega Q_{\phi(x)}(E - \phi(x))d\mu(x)$$

(A1') ϕ is a strict contraction on a closed ball B^* around x^*

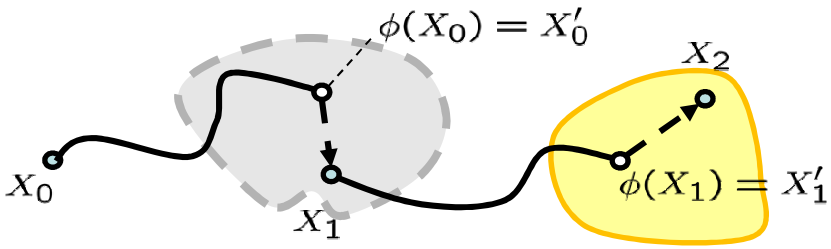
(A2') $\phi : B^* \to B^*$ is a compact map

(A3') $\|Q_x - Q_y\|_{FM} \leq L\|x - y\|$

(A4') $C_x := \text{supp}(Q_x)$ is bounded for all $x \in S$ and $d_H(C_x, C_y) \leq L\|x - y\|$

(replaces (A1) $\text{supp}(Q_v) = [\max(-m_c, -v), 0]$ for all $v > 0$;

In infinite dimensions
-- sketch --



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(A5') $\sup_{y \in C_x} \|y\| < (1 - \theta(1 + L))R^*$ for all $x \in B^*$

'***smallness***', θ: Lipschitz constant of ϕ on B^*, R^*: radius of B^*

In infinite dimensions

Theorem: (Alkurdi, H. Van Gaans, 2013)

Asume that (A1') – (A5') hold. Then P is a *non-expansive Markov operator*, i.e. $\|P\mu - P\nu\|_{FM} \leq \|\mu - \nu\|_{FM}$.

Moreover, P leaves B^* invariant and the restriction of P to $\mathcal{P}(B^*)$ is asymptotically stable. In particular, there exists a unique invariant measure μ^* in $\mathcal{P}(B^*)$ such that

$$\|P^n\mu - \mu^*\|_{FM} \to 0$$

for all $\mu \in \mathcal{P}(B^*)$

Thus, **stability persists** when 'small' random interventions are added *('small' defined by Assumption (A5'))*

In infinite dimensions
-- the fundamental ingredient --

Theorem: (Szarek 1997)

Let (S,d) be a complete separable metric space.
Any non-expansive, locally and globally concentrating Markov operator on S is asymptotically stable.
I.e., there exists a unique invariant measure μ^*, such that for all $\mu\in\mathcal{P}(S)$,

$$\|P^n\mu-\mu^*\|_{FM}\to 0$$

Non-expansive: $\|P\mu-P\nu\|_{FM}\leq\|\mu-\nu\|_{FM}$

(note: Markov operator is non-expansive in $\|\cdot\|_{TV}$)

Globally concentrating:

For every $\varepsilon>0$ and every bounded Borel set $B\subset S$, there exists a bounded Borel set $B'\subset S$ and integer N such that $P^n(B')\geq 1-\varepsilon$ for all $\mu\in\mathcal{P}(S)$ concentrated on B and all $n\geq N$.

In infinite dimensions
-- the fundamental ingredient --

Theorem: (Szarek 1997)

Let (S,d) be a complete separable metric space.
Any non-expansive, locally and globally concentrating Markov operator on S is asymptotically stable.
I.e., there exists a unique invariant measure μ^*, such that for all $\mu \in \mathcal{P}(S)$,

$$\|P^n\mu - \mu^*\|_{FM} \to 0$$

Locally concentrating:

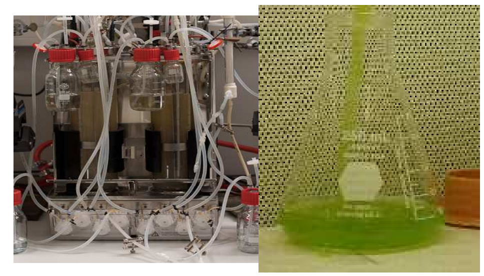
For every $\varepsilon > 0$ there exists $\alpha > 0$, such that for every bounded Borel set $B \subset S$, there exists a Borel set C with $\mathrm{diam}(C) < \varepsilon$ and integer N, such that $P^n\mu(C) \geq \alpha$ for all $n \geq N$ and $\mu \in \mathcal{P}(S)$ concentrated on B.

How to check the technical conditions?

The philosophy is the same as for the finite dimensional (1D) case:

– Consider the ***support evolution map***, or ***Markov set function***

$$\Psi_P(E) := \mathrm{Cl}\left(\bigcup_{x\in E} \mathrm{supp}(P\delta_x)\right)$$



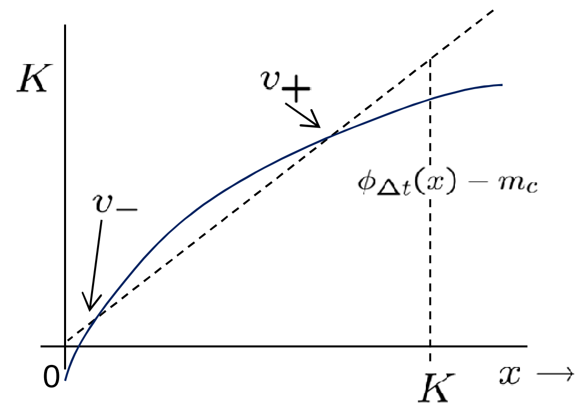
(Recall the 1D example – ‘sampling / harvesting’:

$$\psi(x) := [\phi_{\Delta t}(x) - m_c]^+$$

$$\mathrm{supp}(P^n\delta_x) = [\psi^n(x), \phi_{n\Delta t}(x)]$$

In this case,

$$\Psi_P([a,b]) = [\psi(a), \phi_{\Delta t}(b)]$$



$\phi_{n\Delta t}(b) \to K$ if $b > 0$

$\psi^n(a) \to v_+$ if $a > v_-$ $\psi^n(a) \to 0$ if $a < v_-$

In infinite dimensions
-- a similar approach --

How to check the technical conditions?

The philosophy is the same as for the finite dimensional (1D) case:

– Consider the ***support evolution map***, or ***Markov set function***

$$\Psi_P(E) := \mathrm{Cl}\left(\bigcup_{x\in E} \mathrm{supp}(P\delta_x)\right)$$

– Show that it is a strict contraction in Hausdorff distance d_H

$$d_H(\Psi_P(A), \Psi_P(B)) \leq \theta d_H(A,B)$$

with $0 \leq \theta < 1$.

$$d_H(A,B) := \max(\delta(A,B), \delta(B,A))$$

$$\delta(A,B) := \sup_{x\in A}\inf_{y\in B} d(x,y)$$

– If (S,d) is complete, then so is the space of bounded closed subsets, equipped with d_H

In infinite dimensions -- a similar approach --

How to check the technical conditions?

– Thus, Ψ_P has a unique fixed point E^*, a closed bounded set

Theorem: (Alkurdi, H., Van Gaans 2013)

Assume that (A1')—(A5') hold.

For any $y \in E^*$ and for all $r > 0$, there exists $N \in \mathbb{N}$ and $\alpha > 0$ such that $P^n \delta_x(B(y,r)) \geq \alpha$ for all $x \in S$ and $n \geq N$.

– The **local concentrating property** is an immediate consequence:.

For every $\varepsilon > 0$ there exists $\alpha > 0$, such that for every bounded Borel set $B \subset S$, there exists a Borel set C with $\mathrm{diam}(C) < \varepsilon$ and integer N , such that $P^n\mu(C) \geq \alpha$ for all $n \geq N$ and $\mu \in \mathcal{P}(S)$ concentrated on B .

Outlook

– Assumptions (A1’) – (A5’) hold in a family of models with dispersal and non-overlapping generations.

– So persistence of stability is assured in that infinite dimensional setting *(but now for* $\|\cdot\|_{FM}^{*}$ *instead of* $\|\cdot\|_{TV}$ *)*.

– For further application the **extinction problem** *(for one of the species – the Colorado beetle)* will be considered:

‘Pest control’

– The general case, ‘*random interventions at random times*’ requires further fundamental mathematical research for asymptotic stability results, applicable in that setting *(what are the effects of randomness in the duration of the growth season?)*

Related publications

H. & D.T.H. Worm (2009), *Embedding of semigroups of Lipschitz maps into positive linear semigroups on Banach spaces generated by measures,* Integr. Equ. Oper. Theory **63**, 351-371

D.T.H. Worm (2010), Semigroups on spaces of measures, *PhD thesis*, Leiden University (Supervisor: H.)

T. Alkurdi, H. and O. van Gaans (2013), *Ergodicity and stability of a dynamical system perturbed by stochastic interventions*, To appear in J. Math. Anal. Appl.

T. Alkurdi, H. and O. van Gaans (2013), *Persistence of stability for equilibria of map iterations in Banach spaces under small random perturbations,* submitted.

[redacted]