A large deviations approach to Hamilton-Jacobi scaling limits of PDE models of adaptive evolution of quantitative traits

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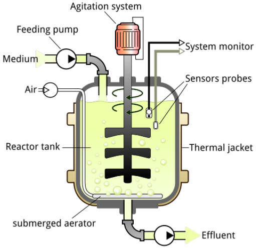
Introduction

Goal of the talk:

- Study general PDE models of evolution, describing the evolution of quantitative phenotypic traits.
- Explain the approach of limit of “concentration” allowing to describe the population dynamics as Dirac mass(es) evolving with time.
- Give an alternative description of the Hamilton-Jacobi limit given by this approach using a probabilistic interpretation of the PDE.
- Discuss extensions of this approach, including the case of a finite trait space, for which the limit can be fully characterized.

Chemostat example



PDE model with r resources: $u(t,x)$ is the density of population with trait $x \in \mathbb{R}$ at time $t \geq 0$

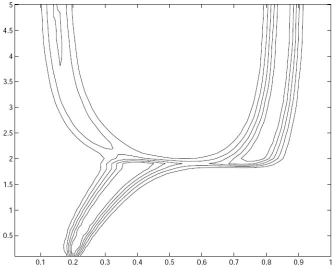
$$\partial_t u(t,x) = u(t,x)\Bigg(\underbrace{\gamma \sum_{i=1}^{r} v_i(t)\eta_i(x)}_{\text{growth}} - \underbrace{1}_{\text{outflow}}\Bigg) + \underbrace{\frac{1}{2}\Delta u(t,x)}_{\text{mutation}}$$

$$\dot{v}_i(t) = \underbrace{c_i}_{\text{inflow}} - \underbrace{v_i(t)}_{\text{outflow}} - \underbrace{v_i(t)\int_{\mathbb{R}} \eta_i(x)u(t,x)\,dx}_{\text{consumption of resource } i}$$

Resources dynamics on a fast time scale

Putting resources dynamics at equilibrium, we obtain the PDE

$$\partial_t u(t,x) = \frac{1}{2}\Delta u(t,x) + u(t,x)\left(\sum_{i=1}^{r} \frac{\gamma c_i \eta_i(x)}{1+\int \eta_i(x) u(t,x)} - 1\right)$$



Competition for two resources

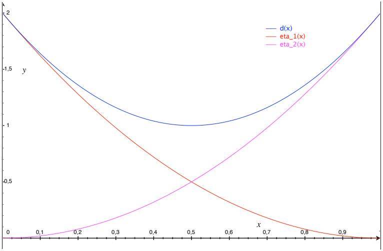
(Diekmann, Jabin, Mischler, Perthame, 2005)

$\rightsquigarrow$ evolutionary branching

An example

Two resources, trait having opposite effects on consumption.

- $K(z)dz = \mathcal{N}(0, \sigma^2)$,
- $d(x) = 1 + 4(x - 1/2)^2$, (minimum at $1/2$), $x \in [0, 1]$,
- $r = 2$ (2 resources), $g_1 = g_2 = 1$,
- $\eta_1(x) = 2(x-1)^2$, $\eta_2(x) = 2x^2$, $x \in [0, 1]$.



General model

$$\partial_t u(t,x) = \frac{1}{2}\Delta u(t,x) + u(t,x) R\left(x, v_t\right), \quad x \in \mathbb{R}^d,\ t \geq 0,$$
$$v_t^i = \int_{\mathbb{R}^d} \eta_i(x) u(t,x)\, dx, \quad 1 \leq i \leq r,$$

where

- $-M \leq \partial_{v_i} R\left(x, v_1, \ldots, v_r\right) \leq -M^{-1}$.
- $\min_{x\in\mathbb{R}^d} R(x,v) > 0$ as soon as $\|v\| < v_{\min}$, and $\max_{x\in\mathbb{R}^d} R(x,v) < 0$ as soon as $\|v\| > v_{\max}$

Small/rare mutations and large time/strong selection

$$\partial_t u^\varepsilon(t,x) = \frac{\varepsilon}{2}\Delta u^\varepsilon(t,x) + \frac{1}{\varepsilon} u^\varepsilon(t,x) R\left(x, v_t^\varepsilon\right),$$

$$u^\varepsilon(0,x) = \exp -\frac{h_\varepsilon(x)}{\varepsilon}, \quad v_t^{\varepsilon,i} = \int_{\mathbb{R}^d} \eta_i(x) u^\varepsilon(t,x)\,dx,$$

where h_ε converges to h in L^∞, and

$$v_{\min} \leq \sum_i \int e^{-h_\varepsilon(x)/\varepsilon} \eta_i(x)\,dx \leq v_{\max}.$$

Diekmann et al., 2005: defining (WKB ansatz)

$$u_\varepsilon(t,x) = \exp\left(\frac{\varphi_\varepsilon(t,x)}{\varepsilon}\right), \quad \partial_t u_\varepsilon = \frac{u_\varepsilon}{\varepsilon}\partial_t \varphi_\varepsilon, \; \Delta u_\varepsilon = \frac{\Delta \varphi_\varepsilon}{\varepsilon} u_\varepsilon + \frac{|\nabla \varphi_\varepsilon|^2}{\varepsilon^2} u_\varepsilon,$$

the PDE becomes

$$\partial_t \varphi_\varepsilon(t,x) = R(x, v_t^\varepsilon) + \frac{1}{2}|\nabla \varphi_\varepsilon(t,x)|^2 + \frac{\varepsilon}{2}\Delta \varphi_\varepsilon$$

Hamilton-Jacobi limit with constraints

This suggests the convergence of φ_ε to a solution of

$$\partial_t\varphi(t,x) = R(x,v_t) + \frac{1}{2}|\nabla\varphi(t,x)|^2,$$
$$\varphi(0,x) = -h(x), \quad v_t^i = \int_{\mathbb{R}^d} \eta_i(x)\mu_t(dx),$$

where $\mu_t(dx)$ is (in some sense) the limit of $u_\varepsilon(t,x)dx$.

Such a convergence and the limit HJ equation were studied in lots of works (Diekmann, Jabin, Mischler, Perthame, 2005; Barles, Perthame, 2007, 2008; Barles, Mirrahimi, Perthame, 2009; C., Jabin, 2011; Lorz, Mirrahimi, Perthame, 2011; Mirrahimi, Roquejoffre, 2016...)

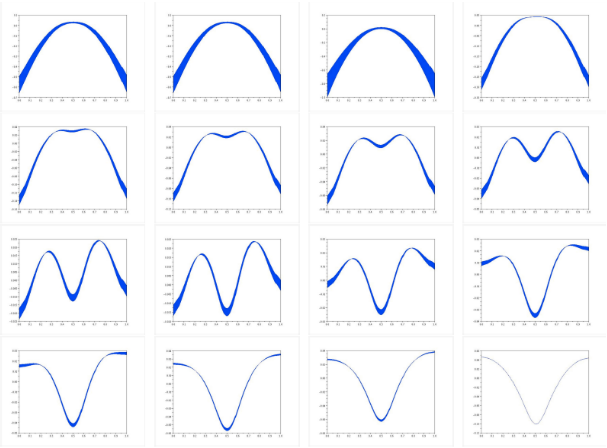
How to characterize μ_t?

- The total population mass remains bounded $\rightsquigarrow$ $\max_x \varphi(t,x) = 0$ for all $t \geq 0$.
- The limit population density at time t is 0 except at the points x where $\varphi(t,x) = 0$ $\rightsquigarrow$ μ_t has support in $\{\varphi(t,\cdot) = 0\}$.
- The measure μ_t has to be metastable, i.e.
  - $R(x, v_t) \leq 0$ for all x such that $\varphi(t,x) = 0$,
  - $R(x, v_t) = 0$ for all x in the support of μ_t.

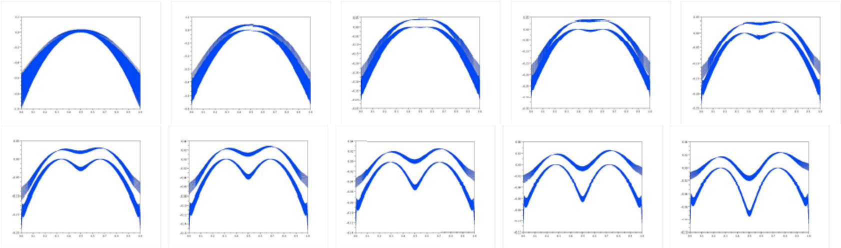
These properties are enough to characterize μ_t from $\{\varphi(t,\cdot) = 0\}$ in the case of a single resources ($r = 1$), but it is only known in particular models for two or more resources (chemostat example, cf. C., Jabin, 2011).

Well-posedness for the HJ equation is a hard problem, only solved in general for a single resource ($r = 1$, cf. Mirrahimi, Roquejoffre, 2016).

Simulation of the PDE in the chemostat example [T. Causseron]



Simulation of HJ in the chemostat example



Back to the chemostat example

$$R(x,v)=\sum_{i=1}^{r}\frac{\gamma c_i\eta_i(x)}{1+v_i}-d(x)$$

The measure μ_t

- has support in $\{x \text{ s.t. } \varphi(t,x)=0\}$
- is metastable: $\forall x\in \mathrm{Supp}(\mu_t),\ R(x,v_t)=0$, where $v_{t,i}=\int \eta_i(x)\mu_t(dx)$

Generically, $\begin{pmatrix}\eta_1(x_1)\\ \vdots \\ \eta_1(x_{r+1})\end{pmatrix},\dots,\begin{pmatrix}\eta_r(x_1)\\ \vdots \\ \eta_r(x_{r+1})\end{pmatrix},\begin{pmatrix}d(x_1)\\ \vdots \\ d(x_{r+1})\end{pmatrix}$ are linearly independent

so $\mathrm{Card}\,\mathrm{Supp}(\mu_t)\leq r$, i.e. no more species than resources can coexist (competitive exclusion principle).

Fitness function

Hamilton-Jacobi equation:

$$\partial_t \varphi(t,x) = R(x, v_t) + \frac{1}{2}|\nabla \varphi(t,x)|^2$$

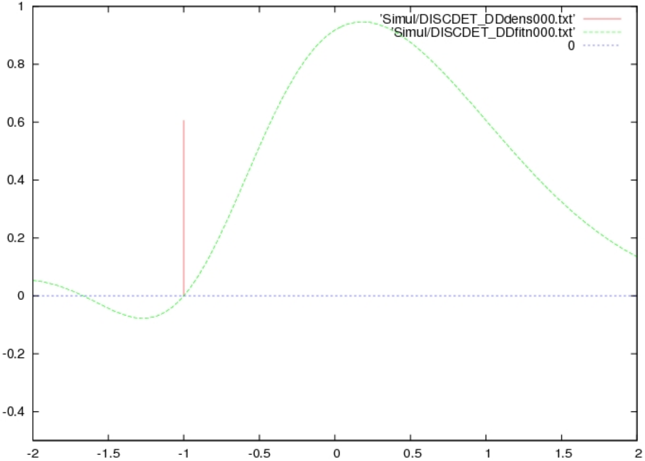
The growth of $\varphi(t,x)$ close to local maxima is governed by the sign of

$$f(x,t) = R(x, v_t),$$

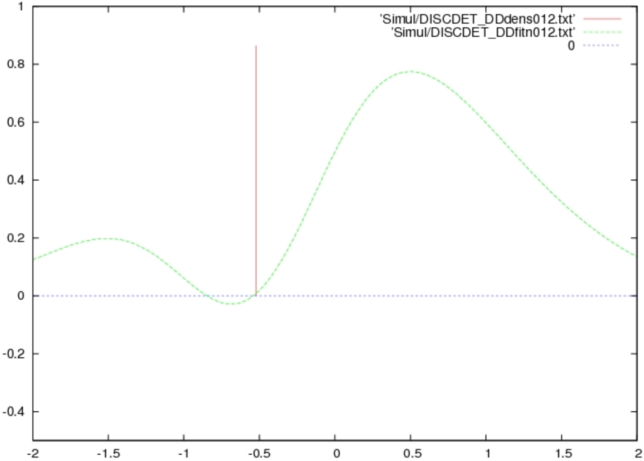
which can be interpreted as the invasion fitness of a (mutant) trait x in the environment v_t implied by the population at time t.

We get the usual picture of hill-climbing process in a fitness landscape that depends on the population state (Metz et al., 1996, Geritz et al., 1997).

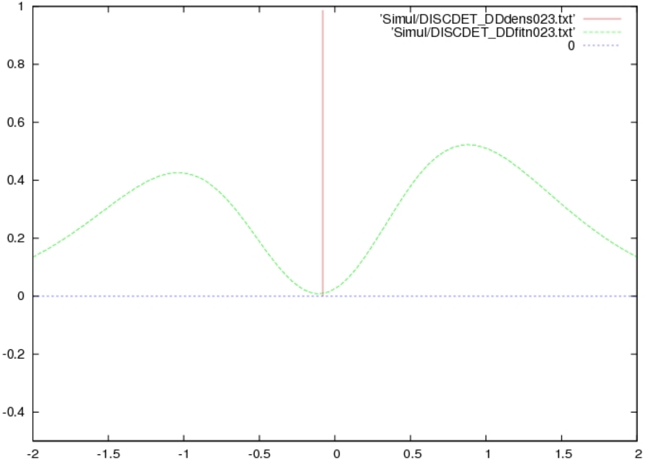
Coevolution with the fitness landscape



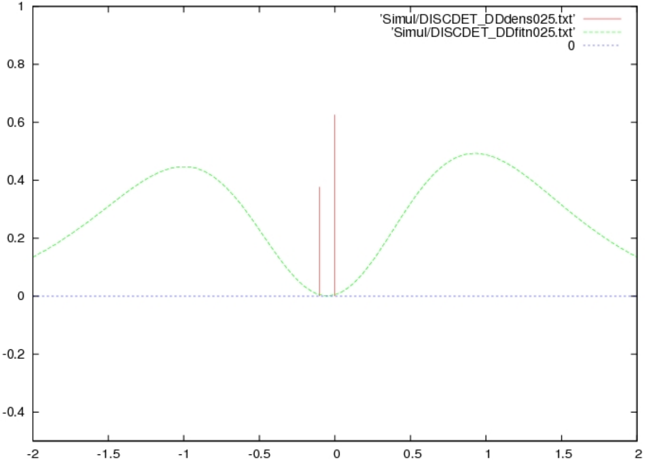
Coevolution with the fitness landscape



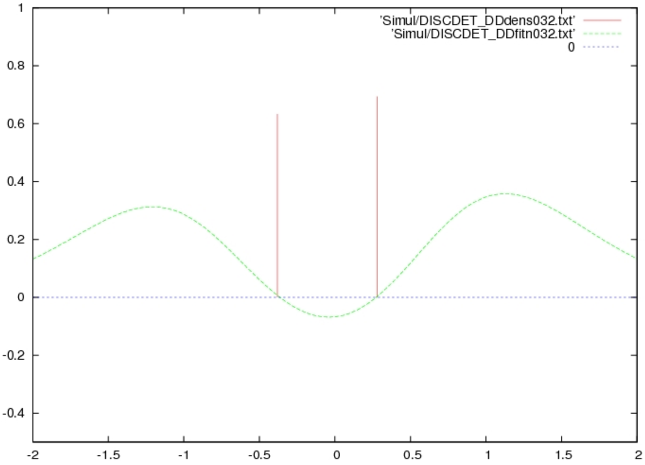
Coevolution with the fitness landscape



Coevolution with the fitness landscape



Coevolution with the fitness landscape



Canonical equation (in dim. 1)

Assuming that μ_t has support $\{\bar{x}(t)\}$

- μ_t metastable implies that $\mu_t = a(t)\delta_{\bar{x}(t)}$ where $a(t)$ is the unique a s.t. $R(\bar{x}(t), a\eta(\bar{x}(t))) = 0$ and $v_{t,i} = a(t)\eta_i(\bar{x}(t))$
- $\varphi(t,x)$ maximal at $\bar{x}(t)$ implies that $\partial_x\varphi(t,\bar{x}(t)) = 0$ and so

$$\partial_t\partial_x\varphi(t,\bar{x}(t)) + \dot{\bar{x}}(t)\partial_{xx}\varphi(t,\bar{x}(t)) = 0$$

- differentiating the HJ equation w.r.t. x at $x = \bar{x}(t)$ gives

$$\partial_t\partial_x\varphi(t,\bar{x}(t)) = \partial_x R(\bar{x}(t), v_t)$$

- hence

$$\dot{\bar{x}}(t) = -\frac{\partial_x R(\bar{x}(t), v_t)}{\partial_{xx}\varphi(t,\bar{x}(t))},$$

where $\partial_x R(\bar{x}(t), v_t)$ is the fitness gradient and $\partial_{xx}\varphi(t,\bar{x}(t))$ is the (scaled) variance of the population distribution.

Probabilistic interpretation of the PDE

We follow ideas from Freidlin (1987, 1992).

Feynman-Kac formula expresses solutions of linear PDEs as expectation of stochastic processes

$$u^{\varepsilon}(t,x) = \mathbb{E}_x\left[\exp\left(-\frac{h_{\varepsilon}(X_t^{\varepsilon})}{\varepsilon} + \frac{1}{\varepsilon}\int_0^t R\left(X_s^{\varepsilon}, v_{t-s}^{\varepsilon}\right) ds\right)\right],$$

where $X_t^{\varepsilon} = x + \sqrt{\varepsilon} B_t$ with B_t Brownian motion.

Strongly suggests to apply Varadhan's lemma!!

Sketch of proof

This can be proved applying Itô's formula between times 0 and t to

$$Y_s = u^\varepsilon(t-s, X_s^\varepsilon)\exp\left(-\frac{1}{\varepsilon}\int_0^s R(X_u^\varepsilon, v_{t-u}^\varepsilon)\,du\right).$$

Setting $\alpha(s,x) = R(x, v_s^\varepsilon)$, we obtain

$$\begin{aligned}
&u^\varepsilon(0, X_t^\varepsilon)\exp\left(\frac{1}{\varepsilon}\int_0^t \alpha(t-u, X_u^\varepsilon)\,du\right) \\
&= u^\varepsilon(t,x) + \int_0^t \nabla u^\varepsilon(t-s, X_s^\varepsilon)\exp\left(\frac{1}{\varepsilon}\int_0^s \alpha(t-u, X_u^\varepsilon)\,du\right) dX_s^\varepsilon \\
&+ \int_0^t \left(-\partial_s u^\varepsilon + \frac{\varepsilon}{2}\Delta u^\varepsilon + \frac{1}{\varepsilon}\alpha u^\varepsilon\right)(t-s, X_s^\varepsilon)\exp\left(\frac{1}{\varepsilon}\int_0^s \alpha(t-u, X_u^\varepsilon)\,du\right).
\end{aligned}$$

This gives the formula taking expectations.

Large deviations principle for Brownian paths

The process $X_t^\varepsilon = x + \sqrt{\varepsilon} B_t$ satisfies a LDP as $\varepsilon \to 0$ (Schilder's theorem):

$$\mathbb{P}_x\left((X_s^\varepsilon)_{s\in[0,t]} \approx (\varphi_s)_{s\in[0,t]}\right) \approx \exp\left(-\frac{1}{\varepsilon} I_t(\varphi)\right), \quad I_t(\varphi) = \frac{1}{2}\int_0^t \|\dot{\varphi}_s\|^2 \, ds.$$

More formally, for all $F \subset \mathcal{C}([0,t], \mathbb{R}^d)$,

$$-\inf_{\varphi\in\mathrm{int}(F)} I_t(\varphi) \leq \liminf_{\varepsilon\to 0} \varepsilon \log \mathbb{P}_x(X^\varepsilon \in F)$$
$$\leq \limsup_{\varepsilon\to 0} \varepsilon \log \mathbb{P}_x(X^\varepsilon \in F) \leq -\inf_{\varphi\in\mathrm{adh}(F)} I_t(\varphi).$$

Varadhan's lemma

Varadhan's lemma is a version of Laplace's principle: for all $f : [0,1] \to \mathbb{R}$ continuous,

$$\int_0^1 e^{\frac{1}{\varepsilon}f(x)}\,dx \approx \exp\left(\frac{1}{\varepsilon}\sup_{y\in[0,1]} f(y)\right),$$

or, more formally,

$$\lim_{\varepsilon\to 0}\varepsilon \log \int_0^1 e^{\frac{1}{\varepsilon}f(x)}\,dx = \sup_{y\in[0,1]} f(y).$$

Varadhan's lemma: if $F : \mathcal{C}([0,T],\mathbb{R}^d) \to \mathbb{R}$ is continuous,

$$\mathbb{E}_x\left(e^{\frac{1}{\varepsilon}F(X^\varepsilon)}\right) = \int e^{\frac{1}{\varepsilon}F(\varphi)}\mathbb{P}(X^\varepsilon \in d\varphi) \approx \int e^{\frac{1}{\varepsilon}F(\varphi)}e^{-\frac{1}{\varepsilon}I_t(\varphi)}\,d\varphi,$$

or

$$\lim_{\varepsilon\to 0}\varepsilon \log \mathbb{E}_x\left(e^{\frac{1}{\varepsilon}F(X^\varepsilon)}\right) = \sup_{\varphi \text{ s.t. } \varphi(0)=x}\left(F(\varphi) - I_t(\varphi)\right).$$

Application to our model

In our case,

$$F_\varepsilon(\varphi) = -h_\varepsilon(\varphi_t) + \int_0^t R(\varphi_s, v^\varepsilon_{t-s})\,ds.$$

Need it to converge as $\varepsilon \to 0$ to F continuous.

- $h_\varepsilon \to h$ in L^∞, h Lipschitz,
- to have a continuous limit of

$$\int_0^t R(\varphi_s, v^\varepsilon_{t-s})\,ds = \int_0^t \int_{\mathbb{R}^r} R(\varphi_s, y)\,\delta_{v^\varepsilon_{t-s}}(dy)\,ds,$$

  it is enough to look at weak convergence of measures: up to a subsequence ε_k,

$$\delta_{v_s^{\varepsilon_k}}(dy)\,ds \to \mathcal{M}_s(dy)\,ds.$$

Main result

Theorem

For all $x \in \mathbb{R}^d$ *and* $t \geq 0$,

$$V(t,x) := \lim_{k\to\infty} \varepsilon_k \log u^{\varepsilon_k}(t,x)$$

$$= \sup_{\varphi \ s.t.\ \varphi_0 = x} \left\{ -h(\varphi_t) + \int_0^t \int_{\mathbb{R}^r} R(\varphi_s, y) \mathcal{M}_{t-s}(dy)\, ds - \frac{1}{2} \int_0^t \|\dot{\varphi}_s\|^2 ds \right\},$$

$V(0,x) = -h(x)$ *and* $V(t,x)$ *is locally Lipschitz in* $\mathbb{R}_+ \times \mathbb{R}^d$.

Interpretation: biologically, the optimal function φ may be thought of as the trait of the ancestral lineage of the dominant individuals at time t.

Link with the HJ problem

When $r = 1$, using the results of Lorz, Mirrahimi, Perthame (2011), we deduce that $\mathcal{M}_t$ is a Dirac mass and $V(t,x) = \varphi(t,x)$, where

$$\partial_t \varphi(t,x) = \int_{\mathbb{R}} R(x,y)\mathcal{M}_t(dy) + \frac{1}{2}|\nabla\varphi(t,x)|^2.$$

This is the classical variational formulation of Hamilton-Jacobi problems.

Note that, in general, $t \mapsto \mathcal{M}_t$ is not continuous, so we cannot apply the standard results of this theory.

Extensions to other mutation models

Our method applies in general to any mutation operator satisfying a large deviations principle. For example,

$$\partial_t u^\varepsilon(t,x) = \frac{1}{\varepsilon}\int_{\mathbb{R}^d}\left[u^\varepsilon(t,x+\varepsilon z) - u^\varepsilon(t,x)\right]K(z)dz + \frac{1}{\varepsilon}u^\varepsilon(t,x)R\left(x,v_t^\varepsilon\right),$$

where $K:\mathbb{R}^d \to \mathbb{R}_+$ satisfies

$$\int_{\mathbb{R}^d} zK(z)dz = 0 \quad \text{and} \quad \int_{\mathbb{R}^d} e^{a|z|^2}K(z)dz < \infty,\ \forall a > 0.$$

The rate function is

$$I_t(\varphi) = \int_0^t \int_{\mathbb{R}^d}\left(e^{\dot{\varphi}_s z} - 1\right)K(z)dz\,ds$$

In this case, the Hamilton-Jacobi limit was obtained in the chemostat example for any number of resources in C., Jabin (2011).

Finite phenotype space

We consider a finite trait space E, and for all $\varepsilon > 0$, the system of ODEs: for all $i \in E$,

$$\dot{u}^\varepsilon(t,i) = \sum_{j \in E} \left[e^{-T(i,j)/\varepsilon} u^\varepsilon(t,j) - e^{-T(j,i)/\varepsilon} u^\varepsilon(t,i) \right] + \frac{1}{\varepsilon} u^\varepsilon(t,i) R(i, v_t^\varepsilon),$$

with

$$u^\varepsilon(0,i) = \exp -\frac{h_\varepsilon(i)}{\varepsilon}, \quad v_t^{k,\varepsilon} = \sum_{j \in E} u^\varepsilon(t,j) \eta_k(j), \quad \forall 1 \leq k \leq r.$$

Exponentially small rate of mutation $\exp\left(-\frac{T(i,j)}{\varepsilon}\right)$ from state j to i, with $T(i,j) > 0$.

Feynman-Kac representation

We make appear the generator of a Markov process:

$$\dot{u}^\varepsilon(t,i) = \sum_{j\in E} e^{-\frac{T(i,j)}{\varepsilon}}\left(u^\varepsilon(t,j) - u^\varepsilon(t,i)\right) + \frac{1}{\varepsilon} u^\varepsilon(t,i) R_\varepsilon(i, v_t^\varepsilon),$$

where

$$R_\varepsilon(i,v) = R(i,v) + \varepsilon\left(e^{-T(i,j)/\varepsilon} - e^{-T(j,i)/\varepsilon}\right).$$

We have

$$u^\varepsilon(t,i) = \mathbb{E}_i\left[\exp\left(-\frac{h_\varepsilon(X_t^\varepsilon)}{\varepsilon} + \frac{1}{\varepsilon}\int_0^t R_\varepsilon(X_s^\varepsilon, v_{t-s}^\varepsilon)\,ds\right)\right],$$

where X_t^ε is a Markov jump process with $X_0^\varepsilon = i$ and jump rate $e^{-\frac{T(i,j)}{\varepsilon}}$ from i to j.

Feynman-Kac representation and LDP

The processes $(X^\varepsilon)_{\varepsilon>0}$ satisfy a LDP with rate function

$$\begin{aligned} I_t : \mathbb{D}([0,t],E) &\to \mathbb{R}_+ \\ \varphi &\mapsto \sum_{s\leq t} T(\varphi_{s-},\varphi_s), \end{aligned}$$

where we assume $T(i,i)=0$ for all $i\in E$.

Difficulty: the rate function does not have compact level sets
$\rightsquigarrow$ Varadhan's lemma requires some work.

Variational problem

Theorem

Assuming $T(i,j) > 0,\ \forall i \neq j,\ \ T(i,j) + T(j,k) > T(i,k)$, *for all* $i \in E$ *and* $t \geq 0$,

$$V(t,i) := \lim_{k\to\infty} \varepsilon_k \log u^{\varepsilon_k}(t,x)$$

$$= \sup_{\varphi \text{ s.t. } \varphi_0 = i} \left\{ -h(\varphi_t) + \int_0^t \int_{\mathbb{R}^r} R(\varphi_s, y)\mathcal{M}_s(dy)\,ds - \sum_{s\leq t} T(\varphi_{s-}, \varphi_s) \right\}.$$

Well-posedness of this variational problem and the associates HJ equation are accessible in this simpler model.

Further assumptions

For all $A \subset E$, we define the restricted dynamical system without mutations:

$$(S_A) \qquad \dot{u}_i(t) = u_i(t) R_i \left(\sum_{j \in A} \eta_k(j) u_j(t), 1 \leq k \leq r \right), \quad \forall i \in A.$$

We assume that, for all A,

- All eq. of (S_A) are hyperbolic, and (S_A) admits a unique eq. u_A^*, satisfying $R_i \left(\sum_{j \in A} \eta_k(j) u_j(t) \right) < 0$ for all $i \in A$ s.t. $u_{A,i}^* = 0$;
- (S_A) admits a strict Lyapunov function L_A, i.e. $\frac{dL_A(u(t))}{dt} < 0$ for all $t \geq 0$ such that $u(t)$ is not an equilibrium.

These assumptions are satisfied in the chemostat example. General conditions for which this is true are also known for competitive Lotka-Volterra systems (C., Jabin, Raoul, 2010).

A key consequence

Lemma

For all $A \subset E$ and all $\rho > 0$ small enough, the first hitting time $t^*_A(u(0), \rho)$ of the ρ-neighborhood of u^*_A by a solution $u(t)$ to (S_A) satisfies

$$t^*_A(u(0), \rho) \leq C^*_\rho(1 + \sup_{i \in A} -\log u_i(0)).$$

This implies

Proposition

For all $t \geq 0$, there exists $\delta_t > 0$ such that, for all $s \in (t, t + \delta_t)$,

$$\mathcal{M}_s = \delta_{F(\{V(t,\cdot)=0\})}, \quad \text{where } F(A) = \left(\sum_{j \in A} \eta_k(j) u^*_{A,j} \right)_{1 \leq k \leq r}, \ \forall A \subset E$$

and $t \mapsto F(\{V(t, \cdot) = 0\})$ is right-continuous.

Main result in the finite case

Theorem

There exists a unique solution to $V(0,i) = -h(i)$ *and*

$$V(t,i) = \sup_{\varphi \ s.t. \ \varphi_0 = i} \left\{ -h(\varphi_t) + \int_0^t R(\varphi_s, F(\{V(t,\cdot)=0\}))ds - I_t(\varphi) \right\}$$

such that $t \mapsto F(\{V(t,\cdot)=0\})$ *is right-continuous, and this is also the unique solution to* $V(0,i) = -h(i)$ *and*

$$\dot{V}(t,i) = \sup \Big\{ R_j(F(\{V(t,\cdot)=0\})) \quad \textit{for } j \in E \ \ s.t. \ \ V(t,j) - T(j,i) = V(t,i) \Big\}$$

such that $t \mapsto F(\{V(t,\cdot)=0\})$ *is right-continuous.*
In particular, $(\varepsilon \log u^\varepsilon(t,i))_{\varepsilon>0}$ *converges to this unique* $V(t,i)$.

Conclusion

We have proved

- the convergence of $\varepsilon \log u^\varepsilon$ to the variational problem associated to the Hamilton-Jacobi equation with constraints, for any number of resources;
- the well-posedness of the Hamilton-Jacobi and variational problems in the case of finite trait space.

This opens the way to

- well-posedness in continuous trait spaces;
- study of evolutionary branching;
- numerical approximations of the Hamilton-Jacobi equation.