Concentration dynamics in a population model structured in age and a phenotypical trait

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Context

- Asexual population
- Age structure : birth and death rates depend on the age variable
- Trait structure : competition, adaptation and mutations

The age- and trait-structured population model

$$
\begin{cases}
\varepsilon \partial_t n_\varepsilon(t,a,x) + \partial_a n_\varepsilon(t,a,x) + \left(\rho_\varepsilon(t) + d(a,x)\right) n_\varepsilon(t,a,x) = 0 \\
n_\varepsilon(t,a=0,x) = \iint_{\mathbb{R}_+ \times \mathbb{R}^d} \frac{1}{\varepsilon^d} M\left(\frac{x-x'}{\varepsilon}\right) b(a',x') n(t,a',x')\, \mathrm{d}a'\, \mathrm{d}x' \\
\rho_\varepsilon(t) = \iint_{\mathbb{R}_+ \times \mathbb{R}^d} n_\varepsilon(t,a,x) \mathrm{d}a\, \mathrm{d}x, \quad n_\varepsilon(t=0,a,x) = n_\varepsilon^0(a,x) > 0
\end{cases}
$$

Goal : To prove $n_\varepsilon(t,a,x) \underset{\varepsilon \to 0}{\longrightarrow} \rho(t) p(a,x) \delta_{x=\bar{x}(t)}$

Outline

Outline

Motivations

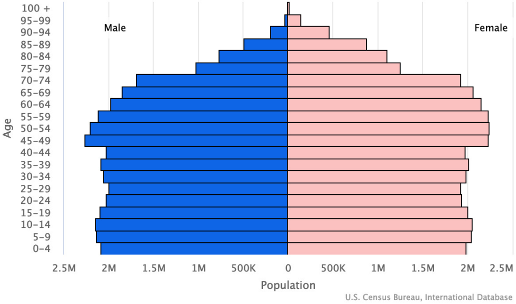


Figure 1: Population pyramid in France in 2020

- demographic : evolution of the age distribution of a human population
- ecological : understanding of the age-dependent birth and death processes of a species

Question : Does the population reach a stable age distribution ?

Age-structured population model

- $a \in \mathbb{R}_+$ age variable
- $n(t, a)$ population density at time t and age a
- $b(a)$, $d(a)$ age-dependent birth and death rates
- $B(t) = \int_{\mathbb{R}_+} b(a)n(t, a)\,\mathrm{d}a$ **fertility or renewal term**

Lotka-McKendrick equation

$$
\begin{cases}
\partial_t n(t,a) + \partial_a n(t,a) + d(a)n(t,a) = 0 \\
n(t, a = 0) = B(t) = \int_{\mathbb{R}_+} b(a)n(t,a)\,\mathrm{d}a \\
n(t = 0, a) = n^0(a) > 0.
\end{cases}
$$

No time-dependency, finite or infinite maximum age, no population migration.

A.G. McKendrick, *Application of mathematics to medical problems* (1926). W. Feller, *On the integral equation of renewal theory* (1941).

Around the age model

On the linear age model

- O. Diekmann, M. Iannelli, B. Perthame, G.F. Webb, ...
- On the stable age distribution : S. Busenberg, M. Iannelli (1985) P. Michel, S. Mischler, B. Perthame (2005), ...
- On the numerical analysis : J. Douglas Jr., F.A. Milner, D. Sulsky, A.M de Roos, ...

Extensions of the linear model

- Nonlinear models : logistic term, Allee effect, ...
- Cell division, maturation structure, size structure, ...
- Epidemics : Kermack-McKendrick SIR model
- etc.

Existence and uniqueness

$S(a) := e^{-\int_0^a d(\sigma)\,\mathrm{d}\sigma}$ survival probability at age a

Method of characteristics :

$$n(t,a) = \begin{cases} B(t-a)S(a), & \text{if } a \le t, \\ n^0(a-t)\dfrac{S(a)}{S(a-t)}, & \text{if } a > t. \end{cases}$$

Renewal integral equation :

$$B(t) = F(t) + \int_0^t K(a)B(t-a)\,\mathrm{d}a,$$

with $K(a) = b(a)S(a)$.

Existence and uniqueness of B

There exists a unique continuous solution to the renewal equation

Proof : Picard iterations method

Results : asymptotic behavior

$$n(t,a) \underset{t \to +\infty}{\sim} e^{\lambda^* t} P(a)$$

with $P(a)$ the stable age distribution

Lotka characteristic equation

$$\widehat{K}(\lambda^*) := \int_0^{+\infty} b(a) S(a) e^{-\lambda^* a} \, \mathrm{d}a = 1$$

$\widehat{K}(0)$ is the net reproduction rate

Two approaches :

- Laplace transform of B : λ^* is a simple pole of $\widehat{B}$.
- Entropy method : λ^* is the principal eigenvalue

$$\int_0^{+\infty} |n(t,a) e^{-\lambda^* t} - \gamma_0 P(a)| \phi(a) \, \mathrm{d}a \to 0$$

Asymptotic behavior : entropy method I

Spectral problem

There exist unique $(\lambda^*, P(a))$ principal eigenelements to

$$\begin{cases} \partial_a P(a) + d(a)P(a) + \lambda^* P(a) = 0, \\ P(0) = \int b(a')P(a')\,\mathrm{d}a' = 1, \quad P(a) > 0. \end{cases}$$

From the differential equation,

$$P(a) = P(0)e^{-\lambda^* a - \int_0^a d(\sigma)\,\mathrm{d}\sigma}.$$

Compute λ^* from the renewal term $P(0) = \int bP$,

$$1 = \int_0^\infty b(a)e^{-\lambda^* a - \int_0^a d(\sigma)\,\mathrm{d}\sigma}\mathrm{d}a.$$

The normalization gives the value of $P(0)$.

Asymptotic behavior : entropy method II

Age profile : $p(t,a) := n(t,a)e^{-\lambda^* t}$

$$\boxed{\partial_t p(t,a) + \partial_a p(t,a) + d(a)p(t,a) + \lambda^* p(t,a) = 0}$$

Then,

$$\partial_t \frac{p(t,a)}{P(a)} + \partial_a \frac{p(t,a)}{P(a)} = 0$$

For $H : \mathbb{R} \to \mathbb{R}$ convex,

$$\frac{\mathrm{d}}{\mathrm{d}t} \int \phi(a) P(a) H\left(\frac{p(t,a)}{P(a)}\right) \mathrm{d}a \leq 0$$

where ϕ is the associated dual eigenvector

$$\begin{cases} -\partial_a \phi(a) + d(a)\phi(a) + \lambda\phi(a) = \phi(0)b(a), \\ \int P(a)\phi(a)\,\mathrm{d}a = 1, \quad \phi(a) \geq 0. \end{cases}$$

P. Michel, S. Mischler, B. Perthame, *General relative entropy inequality: an illustration on growth models*, (2005)

Asymptotic behavior : entropy method III

$$\partial_t \phi(a)P(a)H\left(\frac{p(t,a)}{P(a)}\right) + \partial_a \phi(a)P(a)H\left(\frac{p(t,a)}{P(a)}\right) = - \phi(0)b(a)P(a)H\left(\frac{p(t,a)}{P(a)}\right)$$

By Jensen inequality,

$$\frac{\mathrm{d}}{\mathrm{d}t}\int \phi(a)P(a)H\left(\frac{p(t,a)}{P(a)}\right)\mathrm{d}a \leq 0$$

Convergence to the stage age profile

Assume $|n^0(a)| \leq c_0 P(a)$. Then,

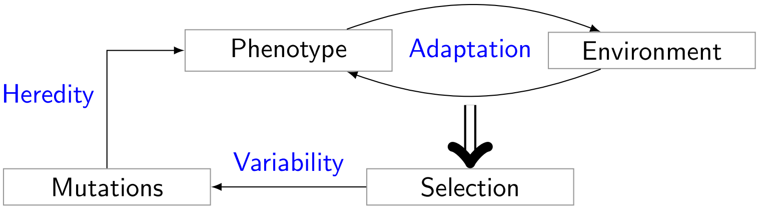
$$\int_0^{+\infty} |n(t,a)e^{-\lambda^* t} - \gamma_0 P(a)|\phi(a)\,\mathrm{d}a \to 0$$

where $\gamma_0 = \int n^0 \phi$

P. Michel, S. Mischler, B. Perthame, *General relative entropy inequality: an illustration on growth models*, (2005)

Outline

Context



- Population structured by a continuous phenotypical trait variable
- Interactions with the environment $\Rightarrow$ non local models
- Dirac mass concentration $\Longleftrightarrow$ selection of the fittest traits

WKB approach

Time rescaling : $t \leftarrow \frac{t}{\varepsilon}$

$$\varepsilon\partial_t n_\varepsilon(t,x) = n_\varepsilon(t,x)R(x,\rho_\varepsilon(t)) + \varepsilon^2\Delta n_\varepsilon(t,x)$$

- Hopf-Cole transform:

$$n_\varepsilon(t,x) = e^{\frac{u_\varepsilon(t,x)}{\varepsilon}}$$

- Equation for u_ε:

$$\partial_t u_\varepsilon(t,x) = |\nabla u_\varepsilon|^2 + R(x,\bar\rho_\varepsilon(t)) + \varepsilon\Delta u_\varepsilon.$$

- When $\varepsilon \to 0$, u_ε converges to u **viscosity solution** to the constrained Hamilton-Jacobi equation

$$\begin{cases} \partial_t u(t,x) = |\nabla u|^2 + R(x,\bar\rho(t)), \\ \max_{x\in\mathbb{R}^d} u(t,x) = 0, \qquad \forall t \geq 0. \end{cases}$$

Diekmann, Jabin, Mischler, Perthame (2005), G. Barles, S. Mirrahimi, B. Perthame (2009), A. Lorz, S. Mirrahimi, B. Perthame (2011)

Biological motivations

→ Extensions to various biological problems, e.g. space, migration between patches, nutrients-consumers, by V. Calvez, P.-E. Jabin, S. Mirrahimi, F. Patout, B. Perthame, A. Lam, etc.

Age and trait structure :

- Demographic evolution
- Antagonist pleiotropic theory : some features with positive effects at early ages and negative effects at older ages, and vice versa

Analysis in two cases : without and with mutations

Work done in collaboration with Samuel Nordmann (U. of Tel Aviv) and Benoît Perthame (Sorbonne Université)

Nordmann, Perthame, Taing (2018)

Outline

Construction of the model

From the renewal equation :

$$\begin{cases} \partial_t n(t,a,x) + \partial_a n(t,a,x) + (d(a,x) + \rho(t))\, n(t,a,x) = 0 \\ n(t,a=0,x) = \displaystyle\iint_{\mathbb{R}_+ \times \mathbb{R}^d} M(x-x') b(a',x') n(t,a',x')\, \mathrm{d}a'\, \mathrm{d}x' \end{cases}$$

- $\rho(t) = \displaystyle\int_{\mathbb{R}_+} \int_{\mathbb{R}} n(t,a,x)\, \mathrm{d}x\, \mathrm{d}a$ competition
- $M(x-x')$ mutation kernel

Rescaling : $t \leftarrow \frac{t}{\varepsilon}, \quad n_\varepsilon(t,a,x) := n(\frac{t}{\varepsilon}, a, x)$

$$\begin{cases} \varepsilon \partial_t n_\varepsilon(t,a,x) + \partial_a n_\varepsilon(t,a,x) + (\rho_\varepsilon(t) + d(x,y))\, n_\varepsilon(t,a,x) = 0 \\ n_\varepsilon(t,a=0,x) = \dfrac{1}{\varepsilon} \displaystyle\iint_{\mathbb{R}_+ \times \mathbb{R}^d} M\left(\frac{x-x'}{\varepsilon}\right) b(a',x') n_\varepsilon(t,a',x')\, \mathrm{d}a'\, \mathrm{d}x' \end{cases}$$

Model without mutations : $M(z) = \delta_0(z)$

$$\begin{cases} \varepsilon \partial_t n_\varepsilon(t,a,x) + \partial_a n_\varepsilon(t,a,x) + \left(\rho_\varepsilon(t) + d(a,x)\right) n_\varepsilon(t,a,x) = 0 \\ n_\varepsilon\left(t, a=0, x\right) = \int_{\mathbb{R}_+} b(a',x) n_\varepsilon(t,a',x)\,\mathrm{d}a' \end{cases}$$

Factorization and Hopf-Cole transform

$$n_\varepsilon(t,a,x) = p_\varepsilon(t,a,x) e^{\frac{u_\varepsilon(t,x)}{\varepsilon}}$$

Age profile p_ε

$$\begin{cases} \varepsilon \partial_t p_\varepsilon + \partial_a p_\varepsilon + d(a,x) p_\varepsilon + (\partial_t u_\varepsilon(t,x) + \rho_\varepsilon(t)) p_\varepsilon = 0, \\ p_\varepsilon(t,0,x) = \int_{\mathbb{R}_+} b(a',x) p_\varepsilon(t,a',x)\,\mathrm{d}a'. \end{cases}$$

Idea : Constrain $\partial_t u_\varepsilon(t,x) + \rho_\varepsilon(t)$

Factorization

Principal eigenelements

Fix $x \in \mathbb{R}$. There exist unique principal eigenelements $(\Lambda(x), P(a,x))$ to

$$\begin{cases} \partial_a P(a,x) + d(a,x)P(a,x) + \Lambda(x)P(a,x) = 0, \\ P(0,x) = \int b(a',x)P(a',x)\,\mathrm{d}a' = 1, \quad P(a,x) > 0. \end{cases}$$

- **We define**

$$\partial_t u_\varepsilon(t,x) = \Lambda(x) - \rho_\varepsilon(t)$$

- **Equation on the age profile** $p_\varepsilon = n_\varepsilon e^{-\frac{u_\varepsilon}{\varepsilon}}$

$$\begin{cases} \varepsilon\partial_t p_\varepsilon + \partial_a p_\varepsilon + d(a,x)p_\varepsilon + \Lambda(x)p_\varepsilon = 0, \\ p_\varepsilon(t,0,x) = \int b(a',x)p_\varepsilon(t,a',x)\,\mathrm{d}a'. \end{cases}$$

Convergence results

Convergence of u_ε and p_ε

- $\rho_\varepsilon(t) \xrightharpoonup[\varepsilon\to 0]{*} \rho(t)$ in $L^\infty(0,\infty)$
- p_ε converges to a multiple of P for a weighted L^p norm, $p \geq 1$
- u_ε converges locally uniformly to a continuous function u solving

$$\begin{cases} \partial_t u(t,y) = \Lambda(y) - \rho(t), & t > 0, y \in \mathbb{R}^n, \\ \sup\limits_{y\in\mathbb{R}} u(t,y) = 0, & \forall t > 0. \end{cases}$$

With u^0 and Λ concave, and defining $\bar{x}(t) = \text{argmax } u(t,\cdot)$

$$n_\varepsilon(t,a,x) \xrightharpoonup[\varepsilon\to 0]{} \rho(t)\frac{1}{\int_x P(a,x)} P(a,x)\delta_{\bar{x}(t)}.$$

Convergence of p_ε

Theorem (convergence of the profile) There exists γ_0 s.t.

$$\int_{\mathbb{R}_+} \left(\frac{p_\varepsilon(t,a,x)}{P(a,x)} - \gamma_0 \right)^2 \mu(a,x)\, \mathrm{d}a \underset{\varepsilon \to 0}{\longrightarrow} 0, \text{ locally uniformly in } (t,x),$$

where $\mu(a,x) = P(a,x)\Phi(a,x)$ is a probability measure.

Proof. Set $v_\varepsilon(t,a,x) = \frac{p_\varepsilon(t,a,x)}{P(a,x)} - \gamma_0$.

- Compute: $\begin{cases} \varepsilon \partial_t v_\varepsilon + \partial_a v_\varepsilon = 0 \\ v_\varepsilon(t, a=0, x) = \int_a v_\varepsilon bP \end{cases}.$
- Introduce the dual eigenfunction $\Phi(a,x)$ of $P(a,x)$.
- Entropy $E_\varepsilon(t,x) = \int_{\mathbb{R}_+} {v_\varepsilon}^2 P(a,x)\Phi(a,x)\, \mathrm{d}a$.
- $\partial_t E_\varepsilon(t,x) \leq 0 \implies 0 \leq E_\varepsilon(t,x) \leq E_\varepsilon(t=0,x) \implies E_\varepsilon(t,x) \underset{\varepsilon}{\to} 0$.

Convergence of u_ε

Constraint on u

u_ε converges locally uniformly towards u, solution to

$$\begin{cases} \partial_t u(t,x) = \Lambda(x) - \rho(t) \\ \sup_{x\in\mathbb{R}} u(t,x) = 0, \forall t \geq 0, \end{cases}$$

- $0 < \underline{r} \leq \rho_\varepsilon(t) \leq \bar{r}, \quad \rho_\varepsilon(t) \xrightarrow[\varepsilon\to 0]{*} \rho(t)$, in L^∞ (after extraction)

$$\boxed{\textbf{Convergence: } u_\varepsilon(t,x) \underset{\varepsilon\to 0}{\longrightarrow} u(t,x) = u^0(x) + t\Lambda(x) - \int_0^t \rho.}$$

- For all $t \geq 0$, $\sup_{x\in\mathbb{R}} u(t,x) = 0$,

$$\boxed{\int_0^t \rho = \sup_y \left[u^0(x) + t\Lambda(x)\right]}$$

Numerical simulations

$$A(a,x) = 1, \qquad b(a,x) = \frac{10x}{1+a^2}, \qquad d(a,x) = x^3(2 + a/3),$$

$$p^0(a,x) = \exp\left(-0.8a\right), \qquad u^0(x) = -\frac{(x-0.5)^2}{2}.$$

Implicit-explicit finite differences scheme

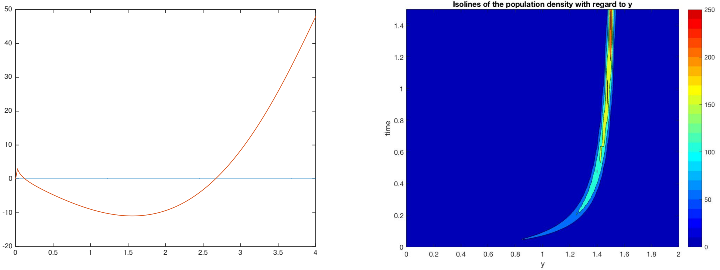


Figure 2: (Left) effective fitness $\Lambda(x)$, (right) total population $t \mapsto \rho_\varepsilon(t)$

Numerical simulations

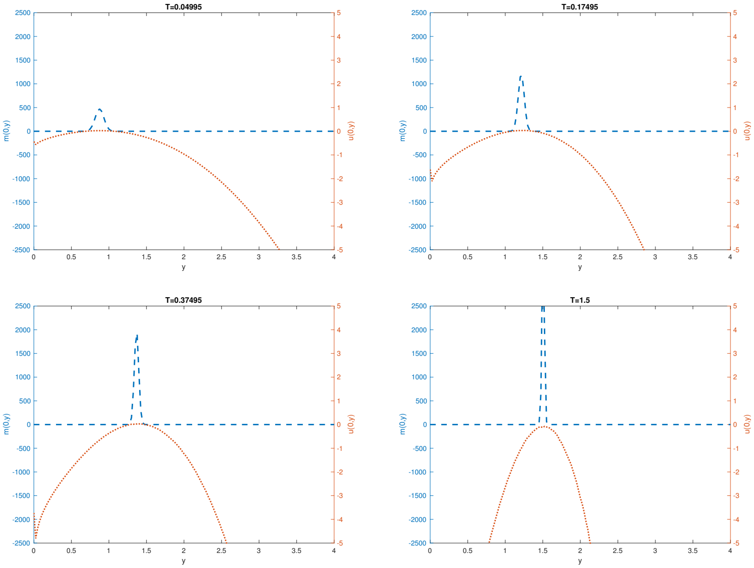


Figure 3: (blue) population of age 0, (red) $u(t,x)$

With mutations : formal computations

- Same approach: $n_\varepsilon(t,a,x) = p_\varepsilon(t,a,x)e^{\frac{u_\varepsilon(t,x)}{\varepsilon}}$,

$$\begin{cases} \varepsilon\partial_t p_\varepsilon + \partial_a p_\varepsilon + d(a,x)p_\varepsilon = (-\partial_t u_\varepsilon(t,x) - \rho_\varepsilon(t))p_\varepsilon, \\ p_\varepsilon(t,0,x) = \iint_{x',a'} \frac{1}{\varepsilon^d} M\left(\frac{x-x'}{\varepsilon}\right) e^{\frac{u_\varepsilon(t,x')-u_\varepsilon(t,x)}{\varepsilon}} b(a',x')p_\varepsilon(t,a',x') \end{cases}$$

- Change of variable $x' \mapsto z = \frac{x'-x}{\varepsilon}$

$$\begin{aligned} p_\varepsilon(t,0,x) &= \int_z M(z)e^{\frac{u_\varepsilon(t,x+\varepsilon z)-u_\varepsilon(t,x)}{\varepsilon}} \int_{a'} b(a',x+\varepsilon z)p_\varepsilon(t,a',x+\varepsilon z)\,\mathrm{d}a\mathrm{d}z \\ &\to \left(\int_z M(z)e^{\partial_x u(t,x)z}\,\mathrm{d}z\right)\left(\int_{a'} b(a',x)p(t,a',x)\,\mathrm{d}a\right) \end{aligned}$$

- Formal limit

$$\begin{cases} \partial_a p + d(a,x)p = (-\partial_t u(t,x) - \rho(t))p, \\ p(t,0,x) = \int_z M(z)e^{\partial_x u(t,x)z}\,\mathrm{d}z \int_{a'} b(a',x)p(t,a',x)\,\mathrm{d}a \end{cases}$$

Hamiltonian

From $\partial_a p + d(a,x)p = (-\partial_t u_\varepsilon(t,x) - \rho_\varepsilon(t))p$,

$$p(t,a,x) = p(t,0,x)e^{-\int_0^a d(\alpha)\mathrm{d}\alpha - (\partial_t u(t,x)+\rho(t))a}.$$

From the renewal term,

$$\frac{1}{\int_{\mathbb{R}} M(z)e^{\partial_x u(t,x)z}\,\mathrm{d}z} = \int_0^{+\infty} b(a,x)e^{-\int_0^a d(\alpha)\mathrm{d}\alpha - (\partial_t u(t,x)+\rho(t))a}\,\mathrm{d}a,$$

$$\widehat{K}(\partial_t u(t,x) + \rho(t)) = \left(\int_z M(z)e^{\partial_x u(t,x)z}\,\mathrm{d}z\right)^{-1}$$

Hamilton-Jacobi equation :

$$\partial_t u(t,x) = H(\partial_x u(t,x)) - \rho(t), \quad \widehat{K}\,(H(p)) = \left(\int_z M(z)e^{pz}\,\mathrm{d}z\right)^{-1}$$

V. Calvez, P. Gabriel, A. Gonzalez Mateos, *Limiting Hamilton-Jacobi equation for the large scale asymptotics of a subdiffusion jump-renewal equation*, (2019)

Convergence results

Spectral problem

Find $\Lambda(x,\eta), P(a,x,\eta)$ solution to

$$\begin{cases} \partial_a P(a,x,\eta) + d(a,x)P(a,x,\eta) + \Lambda(x,\eta)P(a,x,\eta) = 0, \\ P(0,x,\eta) = \eta \displaystyle\int b(a',x)P(a',x,\eta)\,\mathrm{d}a' = 1, \quad P(a,x,\eta) > 0. \end{cases}$$

Results :

- Construction of an approximated problem

$$\begin{cases} \varepsilon\partial_t p_\varepsilon + \partial_a p_\varepsilon + d(a,x)p_\varepsilon = \left(-\partial_t u_\varepsilon(t,x) - \rho_\varepsilon(t)\right) p_\varepsilon, \\ p_\varepsilon(t,0,x) = \eta_\varepsilon(t,x) \displaystyle\int_{a'} b(a',x)p_\varepsilon(t,a',x)\mathrm{d}x \end{cases}$$

- Convergence of $U_\varepsilon(t,x) = u_\varepsilon(t,x) + \int_0^t \rho_\varepsilon$

Outline

In conclusion

Results :

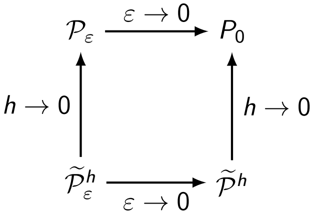
- Factorization : $n_\varepsilon(t,a,x) = p_\varepsilon(t,a,x)e^{\frac{u_\varepsilon(t,x)}{\varepsilon}}$
  - trait profile $e^{\frac{u_\varepsilon(t,x)}{\varepsilon}}$ led by $\Lambda(x)$
  - age profile $p_\varepsilon \to \gamma_0 P$
- Without mutations : convergence with entropy estimates
- With mutations : Hamilton-Jacobi equation on $u + \int_0^t \rho$
  - Definition of an approximated problem $\tilde{\mathcal{P}}_\varepsilon$
  - Construction of $\tilde{u}_\varepsilon$ and $\tilde{p}_\varepsilon$
  - Hamilton-Jacobi equation on $\tilde{u} + \int_0^t \rho$

Recent results

Convergence of p_ε : Nordmann, Perthame (2021)

- estimates of U_ε in $W^{1,r}_{loc}$ with $1 \leq r < \infty$
- $p_\varepsilon \xrightarrow[\varepsilon \to 0]{L^\infty *} \gamma_0 P$

Asymptotic preserving scheme: ongoing work with H. Hivert



Based on the spectral problem : not working

- compute Λ and P
- compute U_ε and $\tilde{p}_\varepsilon$ with extrapolation on η_ε
- $p_\varepsilon = \tilde{p}_\varepsilon + O(\varepsilon)$

Need of another approach

Thank you for your attention !