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# EFFECTS OF AN ADVECTION TERM IN NONLOCAL LOTKA–VOLTERRA EQUATIONS*

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**Abstract.** Nonlocal Lotka–Volterra equations have the property that solutions concentrate as Dirac masses in the limit of small diffusion. In this paper, we show how the presence of an advection term changes the location of the concentration points in the limit of small diffusion and slow drift. The mathematical interest lies in the formalism of constrained Hamilton–Jacobi equations. Our motivations come from previous models of evolutionary dynamics in phenotype-structured populations [R.H. Chisholm, T. Lorenzi, A. Lorz, *et al.*, Cancer Res., 75, 930–939, 2015], where the diffusion operator models the effects of heritable variations in gene expression, while the advection term models the effect of stress-induced adaptation.

**Key words.** Nonlocal Lotka–Volterra equations, Dirac masses, phenotype-structured populations, stress-induced adaptation.

**AMS subject classifications.** 35R09, 45M05, 92D25, 92D15.

## 1. Introduction

We consider the equation

$$\varepsilon\,\partial_t n_\varepsilon(t,x)+\varepsilon\,\nabla_x\cdot(v(x)\,n_\varepsilon(t,x))=R\big(\rho_\varepsilon(t),x\big)\,n_\varepsilon(t,x)+\varepsilon^2\Delta n_\varepsilon(t,x), \tag{1.1}$$

which models the evolutionary dynamics of a well-mixed population structured by the phenotypic traits $x\in\mathbb{R}^d$. Here, the function $n_\varepsilon(t,x)\geq 0$ is the population density which characterises the phenotype distribution of individuals at time $t\in\mathbb{R}_+$, and we note that time has already been rescaled with respect to the parameter $\varepsilon$ in order to study the population dynamics in the limit of many generations [3, 4, 5].

In this mathematical framework, natural selection is driven by the fitness function $R\big(\rho_\varepsilon(t),x\big)$, which models the net proliferation rate of individuals in the environment characterised by the total population density

$$\rho_\varepsilon(t)=\int_{\mathbb{R}^d} n_\varepsilon(t,x)\,dx. \tag{1.2}$$

The Laplace term takes into account heritable variation in gene expression (*i.e.*, epimutations) due to non-genetic instability, whereas the drift term models the effects of stress-induced epimutations [1]. In this setting, the direction of the vector $v$ corresponds with the direction of stress-induced adaptation, while its modulus measures the

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strength of the selective stress. Furthermore, the small parameter $\varepsilon$ incorporates the following two ideas: (i) epimutations are less frequent than proliferation and death events; (ii) non-genetic instability induces epimutations which occur on a timescale slower than that of stress-induced epimutations.

When $v(\cdot)=0$, the solutions of equation (1.1) are known to concentrate as Dirac masses in the limit $\varepsilon\to 0$. In this case, the concentration points are understood as maximum points of the function $u_\varepsilon(t,x)$, which is introduced through a real phase WKB ansatz

$$n_\varepsilon = e^{u_\varepsilon/\varepsilon}, \text{ or equivalently } u_\varepsilon = \varepsilon\ln(n_\varepsilon), \tag{1.3}$$

and satisfies, in the limit $\varepsilon\to 0$, the constrained Hamilton–Jacobi equation presented in [2]. Furthermore, under the concavity assumptions considered in [2, 4, 5], it is possible to prove that there is one single concentration point whose time dynamics is governed by a differential equation that acts as the canonical equation of adaptive dynamics. Here, we show how the inclusion of an advection term influences the dynamics of the Dirac concentration point in the limit $\varepsilon\to 0$.

## 2. Assumptions and main results

We make the following assumptions:

*Assumptions on the function $R$*

- $R$ belongs to $C^2(\mathbb{R}_+\times\mathbb{R}^d)$ and there exists a constant $\rho_M\in\mathbb{R}_+$ such that (fixing the origin in $x$ appropriately):

$$\max_{x\in\mathbb{R}^d} R(\rho_M,x) = 0 = R(\rho_M,0). \tag{2.1}$$

- There exist some positive real constants $\overline{K}_0$, $\underline{K}_1$, $\overline{K}_1$, $\underline{K}_2$, $\overline{K}_2$, and $K_3$ such that for all $\rho\in[0,\rho_M]$:

$$-\underline{K}_1|x|^2 \le R(\rho,x) \le \overline{K}_0 - \overline{K}_1|x|^2, \tag{2.2}$$

$$-2\underline{K}_1 \le D^2R(\rho,x) \le -2\overline{K}_1 < 0, \tag{2.3}$$

$$-\underline{K}_2 \le \frac{\partial R}{\partial \rho} \le -\overline{K}_2, \qquad \Delta R \ge -K_3. \tag{2.4}$$

- Finally,

$$D^3R(\rho,\cdot)\in L^\infty(\mathbb{R}^d), \quad \text{uniformly for } \rho\in[0,\rho_M]. \tag{2.5}$$

*Assumptions on the drift $v$*

- $v$ belongs to $C^2\cap W^{4,\infty}(\mathbb{R}^d)$ and there exists some real constants $A_1, A_2>0$ such that

$$\|\nabla v(x)\| \le A_1, \qquad \left|Tr(D^2v(x))\right| \le 2A_2\frac{1}{1+|x|}. \tag{2.6}$$

*Assumptions on the initial data $n_\varepsilon^0(x)$*

- The initial data $n_\varepsilon^0\in L^1\cap L^\infty(\mathbb{R}^d)$ satisfies $n_\varepsilon^0(x)\ge 0$ a.e. on $\mathbb{R}^d$, and there is a positive real constant $\rho_m$ such that

$$0<\rho_m<\rho_\varepsilon(0) := \int_{\mathbb{R}^d} n_\varepsilon^0(x)\,dx < \rho_M. \tag{2.7}$$

- There exists a function $u_\varepsilon^0$ such that:

$$n_\varepsilon^0(x) = e^{\frac{u_\varepsilon^0(x)}{\varepsilon}} \tag{2.8}$$

with

$$D^3 u_\varepsilon^0 \in L^\infty(\mathbb{R}^d) \quad \text{componentwise uniformly in } \varepsilon. \tag{2.9}$$

With this assumption we can prove a gradient bound $\|\nabla u_\varepsilon\| \leq C_{\nabla u}(1+|x|)$ (cf. equation (2.28)) and we can use the constant $C_{\nabla u}$ to formulate the next assumption

$$\overline{K}_1 - A_2 C_{\nabla u} > 0. \tag{2.10}$$

- There exist some positive real constants $\underline{B}$, $\overline{B}$, $\underline{L}_0$, $\overline{L}_0$, $\underline{L}_1$, and $\overline{L}_1$ such that:

$$-\underline{L}_0 - \underline{L}_1|x|^2 \leq u_\varepsilon^0(x) \leq \overline{L}_0 - \overline{L}_1|x|^2 \tag{2.11}$$

and

$$-2\underline{L}_1 \leq D^2 u_\varepsilon^0 \leq -2\overline{L}_1, \tag{2.12}$$

with

$$\overline{L}_1 \leq \overline{B} \leq \underline{B} \leq \underline{L}_1. \tag{2.13}$$

We will specify $\underline{B}$, $\overline{B}$ in equations (2.32), (2.33).
- Finally,

$$n_\varepsilon^0(x) \xrightarrow[\varepsilon\to 0]{} \rho(0)\delta(x-\bar{x}^0) \quad \text{weakly in the sense of measure.} \tag{2.14}$$

In the framework of these assumptions, we can prove the following

THEOREM 2.1 (Limit $\varepsilon \to 0$). *Let assumptions* (2.1)–(2.4), (2.6), (2.7), *and* (2.13)–(2.12) *hold true. Then, for all* $T>0$*:*

i) A priori bounds on $\rho_\varepsilon(t)$.
*The solutions* $n_\varepsilon$ *to* (1.1) *satisfy*

$$\rho_m \leq \rho_\varepsilon(t) \leq \rho_M \qquad \textit{a.e. on } [0,T], \tag{2.15}$$

*and* $\rho_\varepsilon$ *is uniformly bounded in* $BV(\mathbb{R}_+)$.

ii) Asymptotic behaviour of $\rho_\varepsilon$ and $n_\varepsilon$ for $\varepsilon \to 0$.
*There exists a subsequence of* $\rho_\varepsilon$*, denoted again as* $\rho_\varepsilon$*, such that*

$$\rho_\varepsilon(t) \to \rho(t) \quad \textit{in } L^1_{loc}(\mathbb{R}_+), \quad \textit{as } \varepsilon \to 0, \tag{2.16}$$

*with*

$$\rho_m \leq \rho(t) \leq \rho_M, \qquad \frac{d}{dt}\rho(t) \geq 0. \tag{2.17}$$

*Moreover, weakly in measures,*

$$n_\varepsilon(t,x) \rightharpoonup \rho(t)\delta(x-\bar{x}(t)), \quad \textit{as } \varepsilon \to 0, \tag{2.18}$$

*and the pair* $(\rho(t),\bar{x}(t))$ *satisfies:*

$$R(\rho(t),\bar{x}(t))=0, \quad a.e.\ on\ [0,T]. \tag{2.19}$$

iii) Asymptotic behaviour of $u_\varepsilon(t,x)$ for $\varepsilon\to 0$.

*There exists a subsequence of* $u_\varepsilon$*, denoted again as* $u_\varepsilon$*, such that*

$$u_\varepsilon(t,x)\xrightarrow[\varepsilon\to 0]{} u(t,x) \quad strongly\ in\ L^\infty\big((0,T);W^{1,\infty}_{loc}(\mathbb{R}^d)\big), \tag{2.20}$$

*where* $u(t,x)$ *is a* $C^2$*-function, with* $D^3u(t,\cdot)\in L^\infty(\mathbb{R}^d)$*, that satisfies*

$$\begin{cases} \dfrac{\partial}{\partial t}u(t,x)=R(\rho(t),x)+|\nabla u(t,x)|^2-(v\cdot\nabla u)(t,x), \quad (t,x)\in\mathbb{R}_+\times\mathbb{R}^d,\\ \max\limits_{x\in\mathbb{R}^d}u(t,x)=0=u(t,\bar{x}(t)),\\ u(t=0,x)=u^0(x) \end{cases} \tag{2.21}$$

*in the viscosity sense introduced in [5].*

Theorem 2.2 (Canonical equation). *Let assumptions* (2.1)–(2.12) *hold true. Then,* $\bar{x}(\cdot)$ *belongs to* $W^{1,\infty}(\mathbb{R}_+)$ *and satisfies the following initial value problem*

$$\begin{cases} \dot{\bar{x}}=(-D^2u(t,\bar{x}))^{-1}\cdot\Big(\nabla R(\rho(t),\bar{x})-\nabla(v\cdot\nabla u)(t,\bar{x})\Big), \quad t\in\mathbb{R}_+,\\ \\ \bar{x}(t=0)=\bar{x}^0, \end{cases} \tag{2.22}$$

*where* $\bar{x}^0$ *is defined by assumption* (2.14) *and* $\rho(\cdot)\in W^{1,\infty}(\mathbb{R}_+)$.

Theorem 2.3 (Long-time asymptotics). *Let assumptions* (2.1)–(2.12) *hold true. Then,*

$$\rho(t)\to\rho^\infty \quad and \quad \bar{x}(t)\to\bar{x}^\infty, \quad as\ t\to\infty, \tag{2.23}$$

*and the limits* $\rho^\infty$ *and* $\bar{x}^\infty$ *are identified by the relations*

$$R(\rho^\infty,\bar{x}^\infty)=0, \qquad \Big[\nabla R(\rho^\infty,x)-\nabla(v\cdot\nabla u^\infty)(x)\Big]_{x=\bar{x}^\infty}=0, \tag{2.24}$$

*where* $u^\infty(x)$ *satisfies*

$$\begin{cases} R(\rho^\infty,x)+|\nabla u^\infty(x)|^2-(v\cdot\nabla u^\infty)(x)=0, \quad x\in\mathbb{R}^d,\\ \max\limits_{x\in\mathbb{R}^d}u^\infty(x)=0=u^\infty(\bar{x}^\infty). \end{cases} \tag{2.25}$$

With the additional assumptions (2.6), proofs of the above theorems are similar to those presented in [4, 5] and are left without proof. However, we show that the semi-convexity and the concavity of the initial data is preserved which can be checked with calculations on $D^2u_\varepsilon(t,\cdot)$:

*Proof.* (Bounds on $D^2u_\varepsilon$.) We begin by calculating

$$\partial_t n_\varepsilon=n_\varepsilon\,\partial_t u_\varepsilon/\varepsilon, \quad \nabla n_\varepsilon=n_\varepsilon\,\nabla u_\varepsilon/\varepsilon, \quad \Delta n_\varepsilon=n_\varepsilon\,\Delta u_\varepsilon/\varepsilon+n_\varepsilon\,|\nabla u_\varepsilon|^2/\varepsilon^2. \tag{2.26}$$

Plugging this into equation (1.1), we find that $u_\varepsilon$ satisfies the Hamilton–Jacobi equation

$$\frac{\partial}{\partial t}u_\varepsilon(t,x) = R(\rho_\varepsilon(t),x) + |\nabla u_\varepsilon(t,x)|^2 + \varepsilon\Delta u_\varepsilon(t,x) - (v\cdot\nabla u_\varepsilon)(t,x) - \varepsilon\nabla\cdot v(x). \quad (2.27)$$

In the same way as in [4] Section 8, we obtain the gradient bound. To increase readability we give a brief version here. We write $u_\varepsilon = K - q^2$ with a constant $K$ large enough such that $q(t,x) > C > 0$. Then we obtain

$$\nabla u_\varepsilon = -2q\nabla q \qquad \Delta u_\varepsilon = -2q\Delta q - 2|\nabla q|^2$$

and therefore it follows from equation (2.27) that

$$-2q\partial_t q = R + 4q|\nabla q|^2 - 2\varepsilon q\Delta q - 2\varepsilon|\nabla q|^2 + 2vq\nabla q - \varepsilon\nabla v.$$

Dividing by $-2q$, taking the derivative with respect to $x_i$ and defining $p := \nabla q$, we have

$$\partial_t p_i = -\left(\frac{R}{2q}\right)_{x_i} - 2p_i p^2 - 2qp\cdot\nabla p_i + \varepsilon\Delta p_i + \varepsilon\frac{p\cdot\nabla p_i}{q} - \varepsilon\frac{p^2}{v^2}p_i$$
$$- v_{x_i}\cdot p - v\cdot\nabla p_i + \varepsilon\frac{\nabla\cdot q_{x_i}}{2q} - \varepsilon\frac{\nabla\cdot v}{2q^2}q_i.$$

Since the term of highest order in $p$ on the right hand side is $-2p_i p^2$, we obtain that $p$ is bounded and therefore there is a constant $C_{\nabla u}$ such that

$$\|\nabla u\| \le C_{\nabla u}(1+|x|). \quad (2.28)$$

To prove the concavity results, we only give formal arguments for the limit case. To adapt the argument for the $\varepsilon$-case is purely technical. For a unit vector $\xi$, we use the notation $u_\xi := \nabla_\xi u_\varepsilon$ and $u_{\xi\xi} := \nabla^2_{\xi\xi}u_\varepsilon$ to obtain

$$u_{\xi t} = R_\xi + 2\nabla u\cdot\nabla u_\xi - v_\xi\cdot\nabla u - v\cdot\nabla u_\xi, \quad (2.29)$$
$$u_{\xi\xi t} = R_{\xi\xi} + 2\nabla u_\xi\cdot\nabla u_\xi + 2\nabla u\cdot\nabla u_{\xi\xi} - v_{\xi\xi}\cdot\nabla u - 2v_\xi\cdot\nabla u_\xi - v\cdot\nabla u_{\xi\xi}. \quad (2.30)$$

Along the line of [4], we use the fact that $|\nabla u_\xi| \ge |u_{\xi\xi}|$ and we introduce the definition $\underline{w}(t,x) := \min_\xi u_{\xi\xi}(t,x)$ to achieve

$$\partial_t\underline{w} \ge -2\underline{K}_1 + 2\underline{w}^2 + 2\nabla u\cdot\nabla\underline{w} - v_{\xi\xi}\cdot\nabla u - 2v_\xi\cdot\nabla u_\xi - v\cdot\nabla\underline{w}$$
$$\ge -2\underline{K}_1 + 2\underline{w}^2 + 2\nabla u\cdot\nabla\underline{w} - 2A_2C_{\nabla u} - 2A_1|w| - v\cdot\nabla\underline{w}. \quad (2.31)$$

Defining

$$\underline{B} = \frac{A_1 + \sqrt{A_1^2 + 4(\underline{K}_1 + A_2C_{\nabla u})}}{4}, \quad (2.32)$$

by a comparison principle and assumptions (2.6), (2.12), (2.13), the differential inequality (2.31) gives that if $\underline{B} \le \underline{L}_1$ then $w(t,x) \ge -2\underline{L}_1$ for all times $t$.

The upper bound $-2\overline{L}_1 \ge D^2u(t,x)$ can be obtained similarly with

$$\overline{B} = \frac{-A_1 + \sqrt{A_1^2 + 4(\overline{K}_1 - A_2C_{\nabla u})}}{4}. \quad (2.33)$$

□

In a similar way, we can establish a $L^\infty$-bound (uniform in $\varepsilon$) on the third derivative of $u_\varepsilon(t,\cdot)$.

Moreover, since the function $\rho(t)$ is continuous away from a countable set of discontinuity points, the proof of the relation (2.19) follows the method of Perthame and Barles [5]:

*Proof.* ($R(\rho,\bar{x})=0$.) Let $t^*$ be a continuity point of $\rho(t)$ and $\bar{x}(t^*)$ be a maximum point of $u(t^*,\cdot)$. Using the viscosity subsolution criteria in $(t^*,\bar{x}(t^*))$ and testing against the test function 0, we find

$$R(\rho(t^*),\bar{x}(t^*))\geq 0. \tag{2.34}$$

On the other hand, integrating in time equation (2.21) on the interval $(t^*,t^*+h)$ at the point $x=\bar{x}(t^*)$, we obtain

$$0\geq \frac{u(t^*+h,\bar{x}(t^*))}{h}\geq \frac{1}{h}\int_0^h R(\rho(t^*+s),\bar{x}(t^*))ds+0,$$

which implies, since $t^*$ is a continuity point of $\rho(t)$,

$$0\geq R(\rho(t^*),\bar{x}(t^*)). \tag{2.35}$$

We can then use (2.34) and (2.35) to achieve (2.19). ∎

Finally, the derivation of the canonical equation (2.22) follows the method of Lorz, Mirrahimi, and Perthame [4]:

*Proof.* (Canonical equation.) Since $u_\varepsilon(\cdot,x)$ is concave and smooth, we can define $\bar{x}_\varepsilon(t)$ as the maximum point of $u_\varepsilon(t,\cdot)$ and conclude that $\nabla u_\varepsilon(t,\bar{x}_\varepsilon(t))=0$. This implies that

$$\frac{d}{dt}\nabla u_\varepsilon(t,\bar{x}_\varepsilon(t))=0,$$

and the chain rule gives

$$\frac{\partial}{\partial t}\nabla u_\varepsilon(t,\bar{x}_\varepsilon(t))+D^2u_\varepsilon(t,\bar{x}_\varepsilon(t))\,\dot{\bar{x}}_\varepsilon(t)=0. \tag{2.36}$$

Using equation (2.27) we thus find that, for almost every $t$,

$$\begin{aligned}D^2u_\varepsilon(t,\bar{x}_\varepsilon(t))\,\dot{\bar{x}}_\varepsilon(t)=-\frac{\partial}{\partial t}\nabla u_\varepsilon(t,\bar{x}_\varepsilon(t))&=-\nabla R(\rho_\varepsilon(t),\bar{x}_\varepsilon(t))+\nabla(v\cdot\nabla u_\varepsilon)(t,\bar{x}_\varepsilon(t))\\&\quad-\varepsilon\Delta\nabla u_\varepsilon(t,\bar{x}_\varepsilon(t))+\varepsilon(\nabla(\nabla\cdot v))(\bar{x}_\varepsilon(t)).\end{aligned}$$

Since $R$ belongs to $C^2(\mathbb{R}_+\times\mathbb{R}^d)$, $v$ is a $C^2$-function and $D^3u_\varepsilon$ is bounded uniformly in $\varepsilon$, we can pass to the limit in the above equation and obtain (2.22). ∎

## 3. Numerics

We illustrate the asymptotic results established by theorems 2.1–2.3 by performing numerical simulations in MATLAB. An implicit-explicit finite difference scheme with 3000 points on the interval $[-0.5,1.5]$ is used to solve the mathematical problem defined by equation (1.1), zero Neumann boundary conditions, and the following initial data

$$n_\varepsilon^0(x):=e^{-\frac{(x-0.65)^2}{\varepsilon}}. \tag{3.1}$$

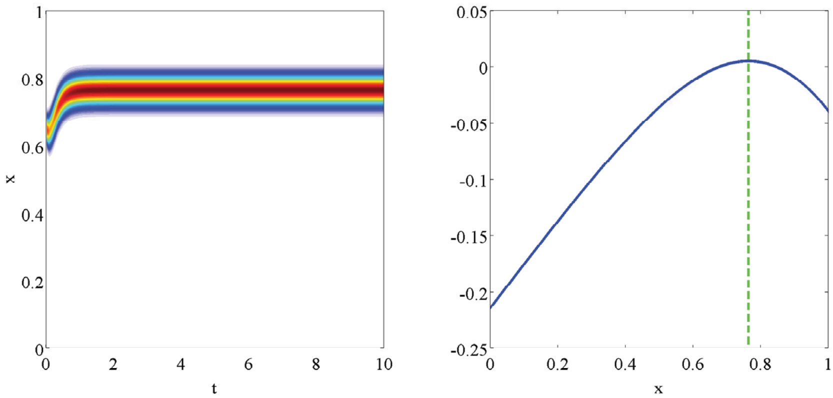


FIG. 3.1. *Dynamics of* $n_\varepsilon(t,x)$ *(left) and profile of* $u_\varepsilon(t,x)$ *at t=10 (right). The dashed line highlights the maximum point of* $n_\varepsilon(t,x)$ *at* $t=10$.

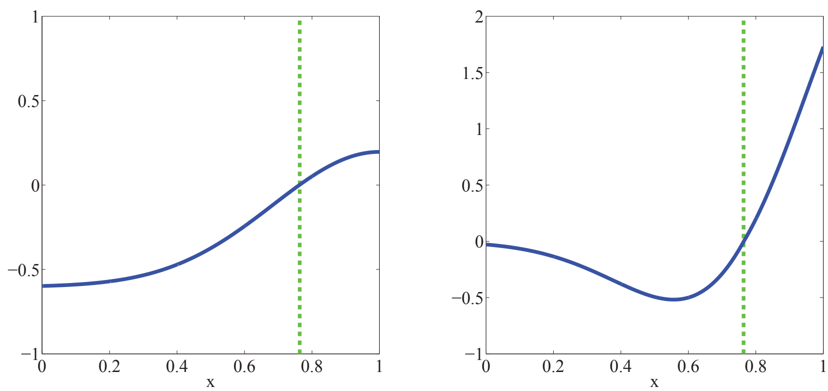


FIG. 3.2. *Profiles of* $R(\rho_\varepsilon(t),x)$ *(left) and* $-\nabla R(\rho_\varepsilon(t),x)+\nabla(v\cdot\nabla u)(t,x)$ *(right) at t=10. The dashed lines highlight the maximum point of* $n_\varepsilon(t,x)$ *at* $t=10$.

We select the interval $[0,10]$ as the time domain (time step $dt=0.0001$), and we define

$$\varepsilon := 0.001, \quad v(\cdot) := -1, \quad R(\rho_\varepsilon(t),x) := 0.1 + 0.8\, e^{-5(x-1)^2} - 0.1\,\rho_\varepsilon(t). \tag{3.2}$$

The results presented in figures 3.1–3.2 show that the solution of equation (1.1) does not concentrate in the point $x=1$, as it would do in the absence of the advection term. Instead, it concentrates in the point that satisfies the relations (2.24).

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