Well-posedness of a structured population model in spaces of measures

Finn Münnich

August 05, 2022

Overview

1. Introduction to structured population models
2. Structured population models in the measure setting
3. Specific class of structured population models
4. Application to an example model

C. Düll et al. *Spaces of Measures and their Applications to Structured Population Models*. 2020

Overview

1. Introduction to structured population models
2. Structured population models in the measure setting
3. Specific class of structured population models
4. Application to an example model

Structured population models

- Used for describing the evolution of cell, animal or human populations with respect to a specific structuring variable (state variable).

Structured population models

- Used for describing the evolution of cell, animal or human populations with respect to a specific structuring variable (state variable).
- Classically studied in the space of Lebesgue integrable functions.

Structured population models

- Used for describing the evolution of cell, animal or human populations with respect to a specific structuring variable (state variable).
- Classically studied in the space of Lebesgue integrable functions.
- L^1-setting does not account for linear combinations of Dirac measures.
  - Cannot be used as initial data in L^1-setting.
  - No description of selection phenomena in L^1-setting.

Overview

Measure setting

- Solution can be interpreted as a state space distribution of the population: If $\mu(t)$ is a solution, then $\int_A \mathrm{d}\mu(t)(x)$ describes individuals of the population which have trait $x \in A$ at time t.

Measure setting

- Solution can be interpreted as a state space distribution of the population: If $\mu(t)$ is a solution, then $\int_A \mathrm{d}\mu(t)(x)$ describes individuals of the population which have trait $x \in A$ at time t.
- Need to clarify what is meant by a solution of a differential equation in a measure space.

Measure setting

- Solution can be interpreted as a state space distribution of the population: If $\mu(t)$ is a solution, then $\int_A \mathrm{d}\mu(t)(x)$ describes individuals of the population which have trait $x \in A$ at time t.
- Need to clarify what is meant by a solution of a differential equation in a measure space.
- Require suitable functional setting and metric.

Functional setting

- Space:
  - A Radon measure is an inner regular and locally finite measure.
  - A measure μ is called nonnegative if $\mu(A) \geq 0$ for all measurable sets $A \subset \mathbb{R}_{\geq 0}$.
  - $\mathcal{M}^+(\mathbb{R}_{\geq 0}) = \{\mu \mid \mu$ is a finite, signed and nonnegative Radon measure$\}$ (no vector space!).

Functional setting

- Space:
  - A Radon measure is an inner regular and locally finite measure.
  - A measure μ is called nonnegative if $\mu(A) \geq 0$ for all measurable sets $A \subset \mathbb{R}_{\geq 0}$.
  - $\mathcal{M}^+(\mathbb{R}_{\geq 0}) = \{\mu \mid \mu$ is a finite, signed and nonnegative Radon measure$\}$ (no vector space!).
- Metric:
  - Bounded Lipschitz functions: $BL(\mathbb{R}_{\geq 0}) := \{f \in C^0(\mathbb{R}_{\geq 0}) \mid \|f\|_\infty < \infty, |f|_{\mathrm{Lip}} < \infty\}$.
  - Flat norm: $\|\mu\|_{BL^*} := \sup\left\{\int_{\mathbb{R}_{\geq 0}} \psi \,\mathrm{d}\mu \mid \psi \in BL(\mathbb{R}_{\geq 0}), \|\psi\|_{BL} \leq 1\right\}$.
  - Flat metric: $\rho_F(\mu, \nu) := \|\mu - \nu\|_{BL^*}$ on $\mathcal{M}^+(\mathbb{R}_{\geq 0})$.

Functional setting

- Space:
  - A Radon measure is an inner regular and locally finite measure.
  - A measure μ is called nonnegative if $\mu(A) \geq 0$ for all measurable sets $A \subset \mathbb{R}_{\geq 0}$.
  - $\mathcal{M}^+(\mathbb{R}_{\geq 0}) = \{\mu \mid \mu$ is a finite, signed and nonnegative Radon measure$\}$ (no vector space!).
- Metric:
  - Bounded Lipschitz functions: $BL(\mathbb{R}_{\geq 0}) := \{f \in C^0(\mathbb{R}_{\geq 0}) \mid \|f\|_\infty < \infty, |f|_{\mathrm{Lip}} < \infty\}$.
  - Flat norm: $\|\mu\|_{BL^*} := \sup \left\{ \int_{\mathbb{R}_{\geq 0}} \psi \, \mathrm{d}\mu \mid \psi \in BL(\mathbb{R}_{\geq 0}), \|\psi\|_{BL} \leq 1 \right\}$.
  - Flat metric: $\rho_F(\mu, \nu) := \|\mu - \nu\|_{BL^*}$ on $\mathcal{M}^+(\mathbb{R}_{\geq 0})$.

$\Rightarrow$ We choose the positive cone $\mathcal{M}^+(\mathbb{R}_{\geq 0})$ together with the flat metric as functional setting.

Overview

Linear model with transport term

We consider the following linear population model

$$\begin{cases} \partial_t \mu_t + \partial_x(b\mu_t) = c\mu_t & \text{in } [0,T] \times \mathbb{R}_{\geq 0}, \\ b(0)D_\lambda \mu_t(0) = \int_{\mathbb{R}_{\geq 0}} a \, \mathrm{d}\mu_t & \text{in } [0,T], \end{cases}$$

with given initial condition $\mu_0 \in \mathcal{M}^+(\mathbb{R}_{\geq 0})$.

Linear model with transport term

We consider the following linear population model

$$\begin{cases} \partial_t \mu_t + \partial_x (b\mu_t) = c\mu_t & \text{in } [0,T] \times \mathbb{R}_{\geq 0}, \\ b(0) D_\lambda \mu_t(0) = \int_{\mathbb{R}_{\geq 0}} a \,\mathrm{d}\mu_t & \text{in } [0,T], \end{cases}$$

with given initial condition $\mu_0 \in \mathcal{M}^+(\mathbb{R}_{\geq 0})$. We call a map $\mu : [0,T] \to \mathcal{M}^+(\mathbb{R}_{\geq 0})$ a measure solution if μ is narrowly continuous w.r.t. t and

$$\int_{\mathbb{R}_{\geq 0}} \varphi(T,x)\,\mathrm{d}\mu_T(x) - \int_{\mathbb{R}_{\geq 0}} \varphi(0,x)\,\mathrm{d}\mu_0(x)$$
$$= \int_0^T \int_{\mathbb{R}_{\geq 0}} \big(\partial_t \varphi(t,x) + b(x)\partial_x \varphi(t,x) + c(x)\varphi(t,x) + a(x)\varphi(t,0)\big)\,\mathrm{d}\mu_t(x)\,\mathrm{d}t$$

for all $\varphi \in C^1([0,T] \times \mathbb{R}_{\geq 0}) \cap W^{1,\infty}([0,T] \times \mathbb{R}_{\geq 0})$.

Well-posedness

Theorem (Theorem 2.19 and Remark 3.41 in book [1])

Suppose model functions a, b and c are sufficiently nice. Then, for any initial measure $\mu_0 \in \mathcal{M}^+(\mathbb{R}_{\geq 0})$, there exists a unique Lipschitz continuous solution $\mu : [0, T] \to (\mathcal{M}^+(\mathbb{R}_{\geq 0}), \rho_F)$. Moreover, the solution is Lipschitz continuous w.r.t. the initial measure as well as the model functions.

[1]: C. Düll et al. *Spaces of Measures and their Applications to Structured Population Models.* 2020

Example

Consider following model (Example 2.1 and 2.10 in book [1])

$$\partial_t \mu_t + \partial_x (b\mu_t) = 0 \text{ in } [0,T] \times \mathbb{R}_{\geq 0},$$
$$D_\lambda \mu_t(0) = 0 \text{ in } [0,T],$$
$$\mu_0 = \delta_0$$

with a constant transport coefficient $b > 0$.

[1]: C. Düll et al. *Spaces of Measures and their Applications to Structured Population Models*. 2020

Example

Consider following model (Example 2.1 and 2.10 in book [1])

$$\partial_t \mu_t + \partial_x (b\mu_t) = 0 \text{ in } [0, T] \times \mathbb{R}_{\geq 0},$$
$$D_\lambda \mu_t(0) = 0 \text{ in } [0, T],$$
$$\mu_0 = \delta_0$$

with a constant transport coefficient $b > 0$.
Unique weak solution: $\mu_t = \delta_{bt}$.

[1]: C. Düll et al. *Spaces of Measures and their Applications to Structured Population Models*. 2020

Results from book [1]

In the book, there are also existence, uniqueness and well-posedness results for more general structured population models such as

- the corresponding nonlinear model and
- the corresponding structured population models formulated on a general state space (S, d) that is a proper metric space.

[1]: C. Düll et al. *Spaces of Measures and their Applications to Structured Population Models*. 2020

Overview

Model in L^1-setting

Originates from [2] as a clonal selection model and was extended in [3] to account for mutation.

$$
\begin{aligned}
\frac{\partial}{\partial t} u(t,x) &= B(x,\rho(t),0)u(t,x),\\
\frac{\partial}{\partial t} v(t,x) &= A(x,\rho(t))u(t,x) - \theta v(t,x),\\
u(0,x) &= u^0(x),\\
v(0,x) &= v^0(x),
\end{aligned}
$$

where $x \in \Omega \subset \mathbb{R}$, $\varepsilon, \theta \in \mathbb{R}_{>0}$ and $\rho(t) = \int_\Omega v(t,x)\,\mathrm{d}x$.

---

[2]: J.-E. Busse, P. Gwiazda, and A. Marciniak-Czochra. Mass concentration in a nonlocal model of clonal selection. In: *Journal of Mathematical Biology* (2016)

Model in L^1-setting

Originates from [2] as a clonal selection model and was extended in [3] to account for mutation.

$$\begin{aligned}
\frac{\partial}{\partial t} u(t,x) &= B(x,\rho(t),\varepsilon)u(t,x) + \varepsilon \int_\Omega \kappa(x,y)u(t,y)\,\mathrm{d}y,\\
\frac{\partial}{\partial t} v(t,x) &= A(x,\rho(t))u(t,x) - \theta v(t,x),\\
u(0,x) &= u^0(x),\\
v(0,x) &= v^0(x),
\end{aligned}$$

where $x \in \Omega \subset \mathbb{R}$, $\varepsilon, \theta \in \mathbb{R}_{>0}$ and $\rho(t) = \int_\Omega v(t,x)\,\mathrm{d}x$.

[3]: J.-E. Busse, S. Cuadrado, and A. Marciniak-Czochra. Local asymptotic stability of a system of integro-differential equations describing clonal evolution of a self-renewing cell population under mutation. In: *Journal of Mathematical Biology* (2020)

Model in measure setting

In the measure setting, we have

$$\begin{aligned}\partial_t \mu_t &= B(\cdot, \nu_t(\Omega), \varepsilon)\mu_t + \varepsilon \int_\Omega \eta(y)\, \mathrm{d}[\mu(t)](y),\\ \partial_t \nu_t &= A(\cdot, \nu_t(\Omega))\mu_t - \theta \nu_t,\\ \mu_0 &= \mu^0,\\ \nu_0 &= \nu^0,\end{aligned}$$

where $\eta(y)(M) = \int_M \kappa(x, y)\, \mathrm{d}x$ for a Borel set $M \subset \Omega$.

Results in measure setting

- Basic clonal selection model (see [4, Section 2.7])
  - Existence of a unique global-in-time solution $(\mu, \nu) \in C^1([0, \infty), \mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega))$.
  - $(\mu(t), \nu(t))$ converges w.r.t. the flat metric to a Dirac measure as t tends to infinity.

[4]: J.-E. Busse. Asymptotic behaviour of a system of integro-differential equations describing leukemia. PhD thesis. Ruprecht-Karls-Universität Heidelberg, 2017

Results in measure setting

- Basic clonal selection model (see [4, Section 2.7])
  - Existence of a unique global-in-time solution $(\mu, \nu) \in C^1([0, \infty), \mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega))$.
  - $(\mu(t), \nu(t))$ converges w.r.t. the flat metric to a Dirac measure as t tends to infinity.
- Selection-mutation model (see [5])
  - Existence and uniqueness of a measure solution (μ, ν) in $\mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega)$.
  - Solution is continuous with respect to initial conditions and model functions.

[5]: F. Münnich. *Well-posedness of a structured population model of leukemia evolution in spaces of measures*. Master thesis, Ruprecht Karl University of Heidelberg. 2022

Results in measure setting

- Basic clonal selection model (see [4, Section 2.7])
  - Existence of a unique global-in-time solution $(\mu, \nu) \in C^1([0, \infty), \mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega))$.
  - $(\mu(t), \nu(t))$ converges w.r.t. the flat metric to a Dirac measure as t tends to infinity.
- Selection-mutation model (see [5])
  - Existence and uniqueness of a measure solution (μ, ν) in $\mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega)$.
  - Solution is continuous with respect to initial conditions and model functions.
- For more information about the role of self-renewal see [6].

---

[6]: T. Stiehl and A. Marciniak-Czochra. Stem cell self-renewal in regeneration and cancer: Insights from mathematical modeling. In: *Current Opinion in Systems Biology* 5 (2017), pp. 112–120

References

[1] C. Düll, P. Gwiazda, A. Marciniak-Czochra, and J. Skrzeczkowski. *Spaces of Measures and their Applications to Structured Population Models*. 2020.

[2] J.-E. Busse, P. Gwiazda, and A. Marciniak-Czochra. Mass concentration in a nonlocal model of clonal selection. In: *Journal of Mathematical Biology* (2016).

[3] J.-E. Busse, S. Cuadrado, and A. Marciniak-Czochra. Local asymptotic stability of a system of integro-differential equations describing clonal evolution of a self-renewing cell population under mutation. In: *Journal of Mathematical Biology* (2020).

[4] J.-E. Busse. Asymptotic behaviour of a system of integro-differential equations describing leukemia. PhD thesis. Ruprecht-Karls-Universität Heidelberg, 2017.

[5] F. Münnich. *Well-posedness of a structured population model of leukemia evolution in spaces of measures*. Master thesis, Ruprecht Karl University of Heidelberg. 2022.

[6] T. Stiehl and A. Marciniak-Czochra. Stem cell self-renewal in regeneration and cancer: Insights from mathematical modeling. In: *Current Opinion in Systems Biology* 5 (2017), pp. 112–120.