Unification of ODEs and transport PDEs inspired by models of cellular dynamics

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joint work with
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Partial Differential Equations
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INNOVATIVE ECONOMY
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Discrete versus continuous cellular dynamics

Discrete – a stochastic process described by ODEs:

Feedback signal

$$\frac{d}{dt} n_i(t) = \left(p_i(v(t)) - c_i(v(t))\right) n_i(t) + c_{i-1}(v(t)) n_{i-1}(t)$$

proliferation

differentiation

Continuous – a deterministic process described by transport PDEs:

$$\frac{\partial n(t,x)}{\partial t} + \frac{\partial (g(v(t),x) n(t,x))}{\partial x} = p(v(t,x)) n(t,x)$$

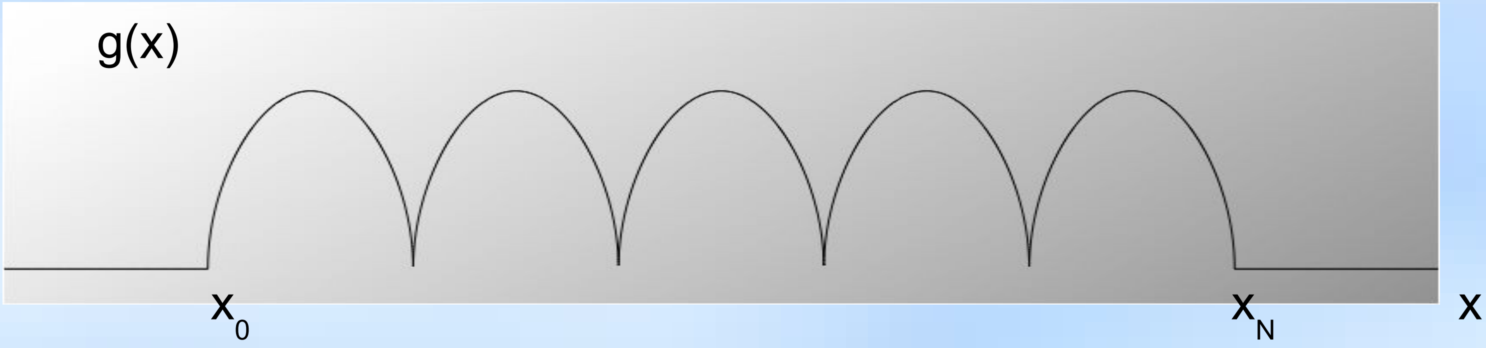
differentiation

proliferation

Disadvantages of both approaches

- Unphysical infinite-speed effects in purely discrete models
- Lack of semitrivial steady states in purely continuous models
- Purely continuous models are not a limit of discrete (cell cycle)
- Inelegance by dealing with coupled ODE-PDE models

Solution: hybrydization into a purely continuous setting of transport equations with vanishing at some points and nonlipschitz velocity and constitutive relations



Distributional solutions in measures of transport equations with nonlipschitz velocity

$$\partial_t \mu + \partial_x (g(v(t), x)\mu) = p(v(t), x)\mu \quad \text{in} \quad D'([0,\infty) \times \mathbb{R})$$

$$g(v(t), x)\frac{d\mu^{ac}(t)}{dL^1}(x_i^+) = c_i(v(t)) \int_{\{x_i\}} d\mu(t), \qquad i = 0, \dots, N$$

$$\mu(0) = \mu_0$$

Initial condition

Constitutive relations

Feedback from the last point $v(t) = \int_{\{x_N\}} d\mu(t)$

Implications of vanishing x-nonlipschitz velocity

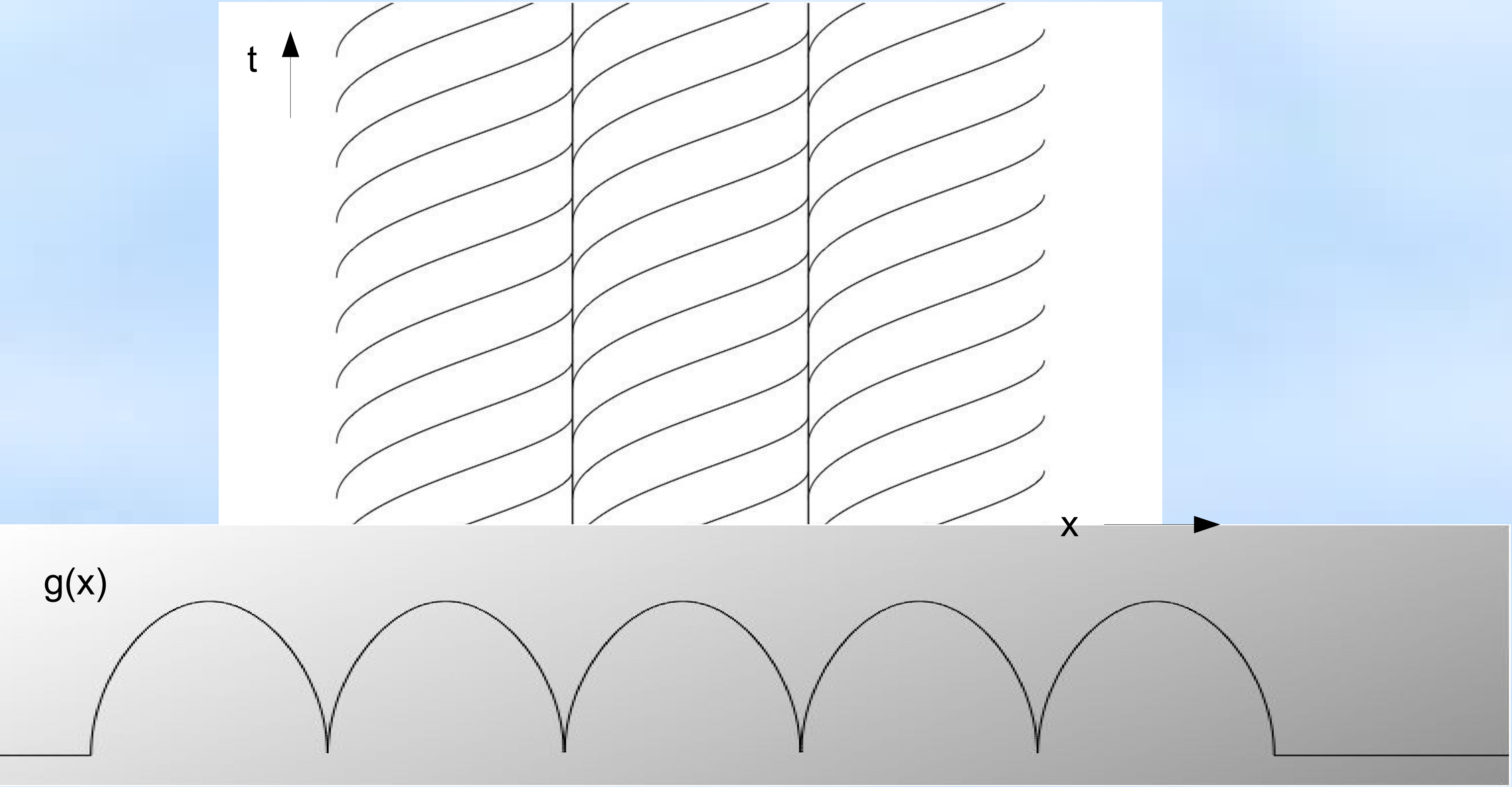
$$g(v(t),x)=g_1(v(t))g_2(x)$$

g_1: Lipschitz, bounded function of its argument

g_2: satisfies $\int \frac{dx}{g_2(x)} < \infty$

- Even if the initial measure is atom-free, the solution develops concentrations at zeroes of g
- The characteristics are nonunique and branch at zereos of g thus defining possible trajectories for every cell
- Constitutive relations define the relative differentiation rate thus allowing to define unique distributional solutions in measures which are continuous in a suitable metric (flat metric on the space of bounded Radon measures)

Nonunique characteristics

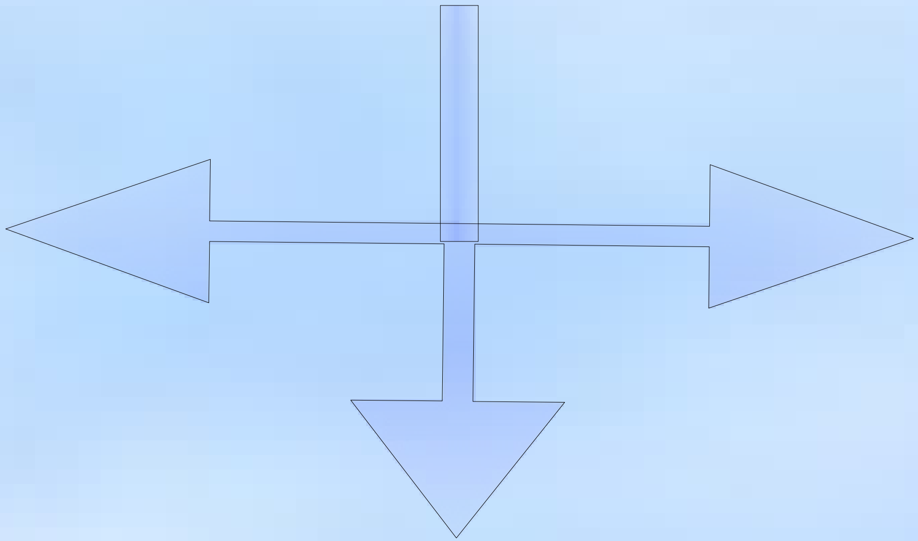


Toy-models (1) - nonuniqueness

$$\partial_t \mu + \partial_x \left(1_{x \neq x_0} \mu \right) = 0$$

$$\mu(0) = \delta_0$$

$$\mu^{null}(t) = \delta_0(x)$$



$$\mu^{\infty}(t) = \delta_t(x)$$

$$\mu^1(t) = e^{-t}\delta_0(x) + e^{(x-t)} 1_{(0,t]}(x)$$

Toy models (2) – stationary solutions

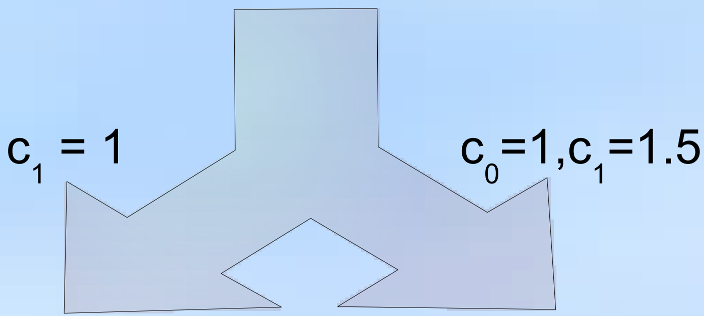
$$\partial_t \mu + \partial_x \left(1_{(0,1)}(x)\, \mu \right) = \left(p\, 1_0(x) - d\, 1_1(x) \right) \mu$$

A stationary solution

$$\mu = \delta_0(x) + p\, 1_{(0,1)}(x) + \frac{p}{d} \delta_1(x)$$

Toy models (3) – semitrivial steady states

$$\partial_t \mu + \partial_x \left(1_{(x \neq x_i)} \mu \right) = \left(1_0(x) + 1_1(x) - 1_2(x) \right) \mu$$



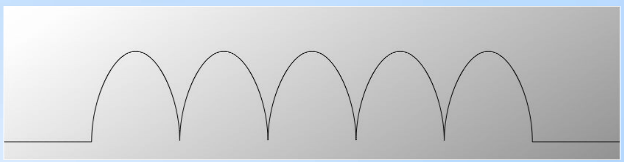
$$\mu = \delta_1(x) + 1_{(1,2)}(x) + \delta_2(x)$$

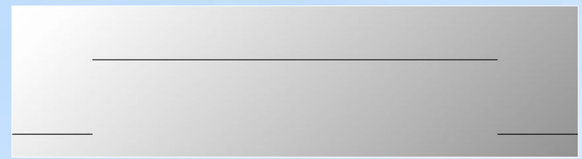
$$\mu = \delta_0(x) + 1_{(0,1)}(x) + 2\,\delta_1(x) + 3\,1_{(1,2)}(x) + 3\,\delta_2(x)$$

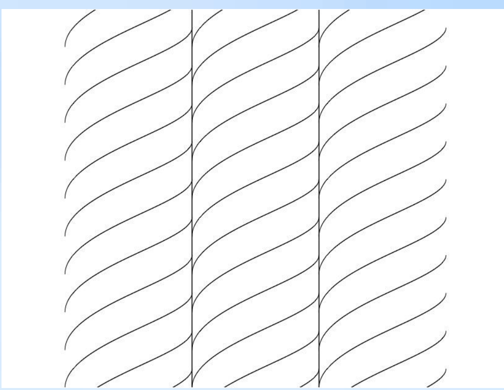
Change of variables – rectification of characteristics

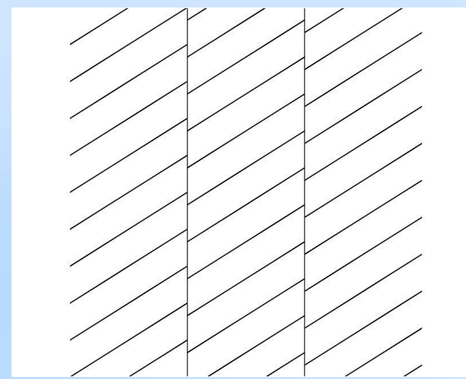
$$x \quad \longrightarrow \quad \int \frac{dx}{g_2(x)}$$

velocity









Simplified assumptions

$$\partial_t \mu + \partial_x (g(v(t), x)\mu) = p(v(t), x)\mu \quad \text{in} \quad D'([0,\infty) \times \mathbb{R})$$

$$g(v(t), x)\frac{d\mu^{ac}(t)}{dL^1}(x_i^+) = c_i(v(t)) \int_{\{x_i\}} d\mu(t), \qquad i = 0, \dots, N$$

$$\mu(0) = \mu_0$$

$$g = g(v(t), x) = g_1(v(t))\, g_2(x)$$

$$g_1(v) \in W^{1,\infty}$$

$$g_1 > 0$$

$$g_2(x) \in C^1((x_{i-1}, x_i)) \cap L^\infty(\mathbb{R})$$

$$g_2 > 0 \text{ in } (x_{i-1}, x_i)$$

$$g_2(x_i) = 0$$

$$\int_{x_{i-1}}^{x_i} \frac{dx}{g_2(x)} < \infty \quad i = 1, \dots, N$$

$$p = p(v(t), x) = p_1(v(t))\, p_2(x)$$

$$p_1(v) \in W^{1,\infty}$$

$$p_2(x) \in L^\infty \cap C^0(\mathbb{R} \setminus \{x_{0,\dots}, x_N\})$$

$$c_i = c_i(v) \in W^{1,\infty}$$

$$c_N = 0$$

Main Theorem

Under the above assumptions for every Radon measure on R, μ_0 we can find a unique mapping μ: [0,T] -> (Radon measures) which is locally Lipschitz continuous with respect to the flat metric ρ_F.

$$\rho_F(\mu, \nu) = \sup_{\phi \in C^1, \|\phi\|_{W^{1,\infty}} \leq 1} \int \phi \, d(\mu - \nu)$$

Sketch of the proof (existence)

1. Transformation of variables (done)
2. Double-freezing of coefficients

$$\partial_t \mu + \partial_x \left(g_1(t_0) 1_{x \neq x_i} \mu \right) = p_1(t)\, p_2(x)\, \mu \quad \text{in} \quad D'([0,\infty) \times \mathbb{R})$$

$$g_1(t_0) \frac{d\mu^{ac}(t)}{dL^1}(x_i^+) = c_i(t) \int_{\{x_i\}} d\mu(t), \qquad i = 0, \ldots, N$$

$$\mu(0) = \mu_0$$

3. Explicit "from left to right" definition of a solution along characteristics (transport of measure)
4. p_1, g_1, c_i are only in BV what leads to complications by definition and verfication that what we defined is a distributional solution Lipschitz continuous (in flat metric)

Sketch of the proof (existence - unfreezing)

Step 1. Rectification of characteristics with repect to time

$$\partial_t \mu + \partial_x (g_1(t) 1_{x \neq x_i} \mu) = p_1(t) p_2(x) \mu \quad \text{in} \quad D'([0,\infty) \times \mathbb{R})$$

$$g_1(t) \frac{d\mu^{ac}(t)}{dL^1}(x_i^+) = c_i(t) \int_{\{x_i\}} d\mu(t), \qquad i = 0, \ldots, N$$

$$\mu(0) = \mu_0$$

Step 2 (Tricky). Solving (in distribution sense) of the endpoint ODE

$$\frac{dv}{dt} = h(t) + p(x_N, v(t)) v(t), \qquad v(t) = \int_{x_N} d\mu(t) \in BV$$

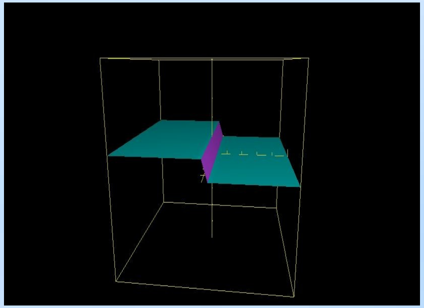
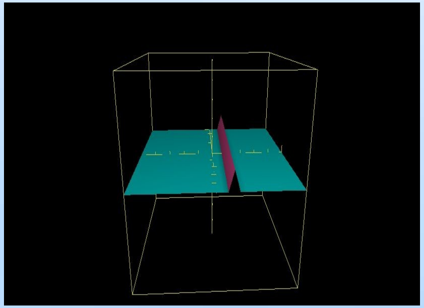
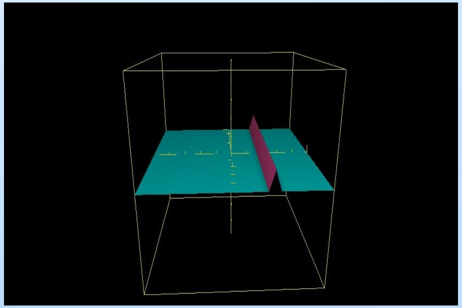
Inflow (measure)

Discretization& Compactness in BV

We are done by the separation of points

Sketch of the proof (uniqueness)

from left to right

(test functions for points x_i)

On intervals: Backward dual equation (taking into account that at xi the measures are equal by induction). Vorsicht(!) Regularity of explicitly found ϕ is insufficient

$$\int \phi(T,x)\,d(\mu_1(T)-\mu_2(T)) = \int_0^T \int_{(x_0,x_1)} (p(t,x)\phi(t,x)+(g_1(t)\partial_x+\partial_t)\phi)\,d(\mu_1(t)-\mu_2(t))\,dt$$

Regularization + passage to the limit, the problematic term:

$$p(t,x)(\phi(t,x)*\rho^{\epsilon})-(p(t,x)\phi(t,x))*\rho^{\epsilon}\to 0$$

At x_N(for v(t))tricky analysis of jumps of the first in time supposed difference of solutions

1. exclude different jumps. 2. if jumps are equal or nonexistent – L^1 contraction

Regularizing effects at quasistationary point x_i

→ When passing through a point x_i the solution becomes more regular (once integrated)

→ This means that after some time the whole solution becomes more regular than initial measures

Perspectives

- Branching
- Disappearance of quasistationary points (destabilization)
- Emergence of quasistationary points

biological expertise required!! – the modelled processes have to stem from reality – we have many possibilities

- Stochastic formulation

Thank You very much for your attention

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This work was done during a visit to University of Heidelberg

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