A nonlinear flux–limited diffusion equation arising in the transport of morphogens [1]

José.M. Mazón

Departamento de Análisis Matemàtico
Universitat de València

Workshop International sur les Mathématiques et l'environnement

Essaouira, November 23-24, 2012

[1]Co-authors : F. Andreu, J. Calvo, J. Soler and M. Verbeni

Linear Diffusion $\Rightarrow$ Infinite speed of propagation

Justification. *"Quantitatively the concentration of particles under study lying beneath this infinite tail is neglible"*

From the Qualitatively point of view, as the concentration is being continuously received, the accumulation in time could be significant.

In some bilogical phenomena small concentration are really significant. For instance, in the transport of morphogens

Linear Diffusion $\Rightarrow$ Infinite speed of propagation

Justification. *"Quantitatively the concentration of particles under study lying beneath this infinite tail is neglible"*

From the Qualitatively point of view, as the concentration is being continuously received, the accumulation in time could be significant.

In some bilogical phenomena small concentration are really significant. For instance, in the transport of morphogens

Linear Diffusion $\Rightarrow$ Infinite speed of propagation

Justification. *"Quantitatively the concentration of particles under study lying beneath this infinite tail is neglible"*

From the Qualitatively point of view, as the concentration is being continuously received, the accumulation in time could be significant.

In some bilogical phenomena small concentration are really significant. For instance, in the transport of morphogens

Linear Diffusion

Linear Diffusion $\Rightarrow$ Infinite speed of propagation

Justification. *"Quantitatively the concentration of particles under study lying beneath this infinite tail is neglible"*

From the Qualitatively point of view, as the concentration is being continuously received, the accumulation in time could be significant.

In some bilogical phenomena small concentration are really significant. For instance, in the transport of morphogens

Morphogens

A morphogen is a substance governing the pattern of tissue development, and the positions of the various specialized cell types within a tissue.

It spreads from a localized source and forms a concentration gradient across a developing tissue

In developmental biology a morphogen is rigorously used to mean a signaling molecule that acts directly on cells to produce specific cellular responses dependent on morphogen concentration

The protein Sonic hedgehog homolog (SHH) is the best studied morphogen. It plays a key role in regulating vertebrate organogenesis, such as in the growth of digits on limbs and organization of the brain.

SHH remains important in the adult. It controls cell division of adult stem cells and has been implicated in development of some cancers.

Morphogens

A morphogen is a substance governing the pattern of tissue development, and the positions of the various specialized cell types within a tissue.

It spreads from a localized source and forms a concentration gradient across a developing tissue

In developmental biology a morphogen is rigorously used to mean a signaling molecule that acts directly on cells to produce specific cellular responses dependent on morphogen concentration

The protein Sonic hedgehog homolog (SHH) is the best studied morphogen. It plays a key role in regulating vertebrate organogenesis, such as in the growth of digits on limbs and organization of the brain.

SHH remains important in the adult. It controls cell division of adult stem cells and has been implicated in development of some cancers.

Morphogens

A morphogen is a substance governing the pattern of tissue development, and the positions of the various specialized cell types within a tissue.

It spreads from a localized source and forms a concentration gradient across a developing tissue

In developmental biology a morphogen is rigorously used to mean a signaling molecule that acts directly on cells to produce specific cellular responses dependent on morphogen concentration

The protein Sonic hedgehog homolog (SHH) is the best studied morphogen. It plays a key role in regulating vertebrate organogenesis, such as in the growth of digits on limbs and organization of the brain.

SHH remains important in the adult. It controls cell division of adult stem cells and has been implicated in development of some cancers.

Morphogens

A morphogen is a substance governing the pattern of tissue development, and the positions of the various specialized cell types within a tissue.

It spreads from a localized source and forms a concentration gradient across a developing tissue

In developmental biology a morphogen is rigorously used to mean a signaling molecule that acts directly on cells to produce specific cellular responses dependent on morphogen concentration

The protein Sonic hedgehog homolog (SHH) is the best studied morphogen. It plays a key role in regulating vertebrate organogenesis, such as in the growth of digits on limbs and organization of the brain.

SHH remains important in the adult. It controls cell division of adult stem cells and has been implicated in development of some cancers.

Morphogens

A morphogen is a substance governing the pattern of tissue development, and the positions of the various specialized cell types within a tissue.

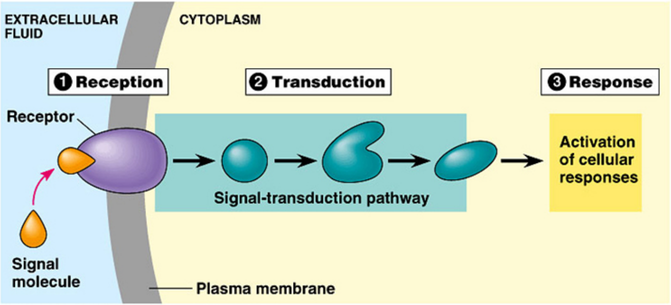
It spreads from a localized source and forms a concentration gradient across a developing tissue

In developmental biology a morphogen is rigorously used to mean a signaling molecule that acts directly on cells to produce specific cellular responses dependent on morphogen concentration

The protein Sonic hedgehog homolog (SHH) is the best studied morphogen. It plays a key role in regulating vertebrate organogenesis, such as in the growth of digits on limbs and organization of the brain.

SHH remains important in the adult. It controls cell division of adult stem cells and has been implicated in development of some cancers.

Morphogen pathway and cellular activation



Sonic Hedgehog (Shh) $\longrightarrow$ GliA

The model by Saha and Schaffer (Development, 2006)

How are morphogens transported? Do they move by linear diffusion (Brownian motion)?

Standard models use linear reaction-diffusion equations

A model by Saha and Schaffer studies patterning in the chick embryo spinal cord, beginning when Shh is first secreted by the floor plate.

A reaction-diffusion equation for the spreading of the morphogen

$$\frac{\partial[Shh]}{\partial t} = D_{Shh}\Delta[Shh] + k_{off}[PtcShh_{out}] - k_{on}[Shh][Ptc_{out}].$$

Plus a set of ordinary differential equations for the concentrations of the proteins involved in the transduction process:

$$[PtcShh_{out}], \quad [PtcShh_{in}], \quad [Ptc_{out}], \quad [Ptc_{in}],$$

$$[Gli1], \quad [Gli3], \quad [Gli3R].$$

The model by Saha and Schaffer (Development, 2006)

How are morphogens transported? Do they move by linear diffusion (Brownian motion)?

Standard models use linear reaction-diffusion equations

A model by Saha and Schaffer studies patterning in the chick embryo spinal cord, beginning when Shh is first secreted by the floor plate.

A reaction-diffusion equation for the spreading of the morphogen

$$\frac{\partial[Shh]}{\partial t} = D_{Shh}\Delta[Shh] + k_{off}[PtcShh_{out}] - k_{on}[Shh][Ptc_{out}].$$

Plus a set of ordinary differential equations for the concentrations of the proteins involved in the transduction process:

$$[PtcShh_{out}], \quad [PtcShh_{in}], \quad [Ptc_{out}], \quad [Ptc_{in}],$$

$$[Gli1], \quad [Gli3], \quad [Gli3R].$$

How are morphogens transported? Do they move by linear diffusion (Brownian motion)?

Standard models use linear reaction-diffusion equations

A model by Saha and Schaffer studies patterning in the chick embryo spinal cord, beginning when Shh is first secreted by the floor plate.

A reaction-diffusion equation for the spreading of the morphogen

$$\frac{\partial [Shh]}{\partial t} = D_{Shh}\Delta[Shh] + k_{off}[PtcShh_{out}] - k_{on}[Shh][Ptc_{out}].$$

Plus a set of ordinary differential equations for the concentrations of the proteins involved in the transduction process:

$$[PtcShh_{out}], \quad [PtcShh_{in}], \quad [Ptc_{out}], \quad [Ptc_{in}],$$

$$[Gli1], \quad [Gli3], \quad [Gli3R].$$

The model by Saha and Schaffer (Development, 2006)

How are morphogens transported? Do they move by linear diffusion (Brownian motion)?

Standard models use linear reaction-diffusion equations

A model by Saha and Schaffer studies patterning in the chick embryo spinal cord, beginning when Shh is first secreted by the floor plate.

A reaction-diffusion equation for the spreading of the morphogen

$$\frac{\partial [Shh]}{\partial t} = D_{Shh}\Delta[Shh] + k_{off}[PtcShh_{out}] - k_{on}[Shh][Ptc_{out}].$$

Plus a set of ordinary differential equations for the concentrations of the proteins involved in the transduction process:

$$[PtcShh_{out}], \quad [PtcShh_{in}], \quad [Ptc_{out}], \quad [Ptc_{in}],$$

$$[Gli1], \quad [Gli3], \quad [Gli3R].$$

Necessity of reducing diffusivity

- Unphysical spreading of the morphogene to all the neural tube soon after secretion.

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Biological Experiments

- The concentration of Shh received by the cells and the time of exposure are of similar relevance. (Briscoe 2007, Nature)

- Shh is transported in relatively big aggregates. (Vincent, Vyas 2008, Cell)

Can we give a transport mechanism that is able to reproduce the recent experimental results?

"Our proposal is to suppress the linear diffusive mechanisms and to use flux limitation instead. Then we are to deal with a non-linear flux-limited reaction-diffusion system".

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Necessity of reducing diffusivity

- Unphysical spreading of the morphogene to all the neural tube soon after secretion.

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Biological Experiments

- The concentration of Shh received by the cells and the time of exposure are of similar relevance. (Briscoe 2007, Nature)

- Shh is transported in relatively big aggregates. (Vincent, Vyas 2008, Cell)

Can we give a transport mechanism that is able to reproduce the recent experimental results?

"Our proposal is to suppress the linear diffusive mechanisms and to use flux limitation instead. Then we are to deal with a non-linear flux-limited reaction-diffusion system".

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Necessity of reducing diffusivity

- Unphysical spreading of the morphogene to all the neural tube soon after secretion.

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Biological Experiments

- The concentration of Shh received by the cells and the time of exposure are of similar relevance. (Briscoe 2007, Nature)

- Shh is transported in relatively big aggregates. (Vincent, Vyas 2008, Cell)

Can we give a transport mechanism that is able to reproduce the recent experimental results?

"Our proposal is to suppress the linear diffusive mechanisms and to use flux limitation instead. Then we are to deal with a non-linear flux-limited reaction-diffusion system".

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Necessity of reducing diffusivity

- Unphysical spreading of the morphogene to all the neural tube soon after secretion.

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Biological Experiments

- The concentration of Shh received by the cells and the time of exposure are of similar relevance. (Briscoe 2007, Nature)

- Shh is transported in relatively big aggregates. (Vincent, Vyas 2008, Cell)

Can we give a transport mechanism that is able to reproduce the recent experimental results?

"Our proposal is to suppress the linear diffusive mechanisms and to use flux limitation instead. Then we are to deal with a non-linear flux-limited reaction-diffusion system".

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

J. Fourier *"Théorie Analytique de la Cheleur"*, 1822

The classical theory of heat conduction is based on Fourier's law

$$\mathbf{q}(t,x) = -\nu \nabla u(t,x),$$

which relates the heat flux $\mathbf{q}$ to the temperature u. Together with the conservation of energy equation,

$$u_t + \mathrm{div}\ \mathbf{q} = 0,$$

this gives the linear parabolic heat equation

$$u_t = \nu \Delta u. \qquad (1)$$

J. Fourier *"Théorie Analytique de la Cheleur"*, 1822

The classical theory of heat conduction is based on Fourier's law

$$\mathbf{q}(t,x) = -\nu \nabla u(t,x),$$

which relates the heat flux $\mathbf{q}$ to the temperature u. Together with the conservation of energy equation,

$$u_t + \mathrm{div}\ \mathbf{q} = 0,$$

this gives the linear parabolic heat equation

$$u_t = \nu \Delta u. \qquad (1)$$

J. Fourier *"Théorie Analytique de la Cheleur"*, 1822

The classical theory of heat conduction is based on Fourier's law

$$\mathbf{q}(t,x) = -\nu \nabla u(t,x),$$

which relates the heat flux $\mathbf{q}$ to the temperature u. Together with the conservation of energy equation,

$$u_t + \mathrm{div}\ \mathbf{q} = 0,$$

this gives the linear parabolic heat equation

$$u_t = \nu \Delta u. \tag{1}$$

Adolf Fick, 1855

Conservation of mass equation

$$u_t + \mathrm{div}\ \mathbf{q} = 0, \tag{2}$$

$u(t,x)$ density of the concentration,
$\mathbf{q}(t,x)$ diffusive flux to the concentration.

Fick's Law $\quad \mathbf{q}(t,x) = -\nu \nabla u(t,x).$

$$u_t = \nu \Delta u. \tag{3}$$

Adolf Fick, 1855

Conservation of mass equation

$$u_t + \mathrm{div}\ \mathbf{q} = 0, \tag{2}$$

$u(t,x)$ density of the concentration,
$\mathbf{q}(t,x)$ diffusive flux to the concentration.

$$\text{Fick's Law} \quad \mathbf{q}(t,x) = -\nu \nabla u(t,x).$$

$$u_t = \nu \Delta u. \tag{3}$$

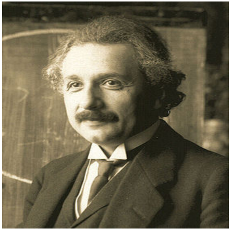
The solution for the Cauchy problem associated to equation (3) with initial data u_0 is given by

$$u(t, \cdot) = G_t \star u_0,$$

where G_t is the Gaussian

$$G_t(x) = (4\pi\nu t)^{-\frac{N}{2}} e^{-\frac{|x|}{4\nu t}}.$$

Starting with u_0 positive with compact support, $u(t, \cdot)$ becomes positive in all $\mathbb{R}^N$ for any time $t > 0$.
The propagation speed for classical linear diffusion based models is infinite.



Annalen der Physik. **19** (1906), 371-381.

The solution for the Cauchy problem associated to equation (3) with initial data u_0 is given by

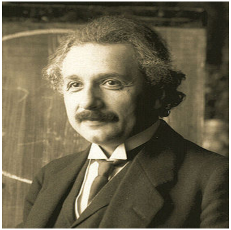
$$u(t,\cdot) = G_t \star u_0,$$

where G_t is the Gaussian

$$G_t(x) = (4\pi\nu t)^{-\frac{N}{2}} e^{-\frac{|x|}{4\nu t}}.$$

Starting with u_0 positive with compact support, $u(t,\cdot)$ becomes positive in all $\mathbb{R}^N$ for any time $t > 0$.

The propagation speed for classical linear diffusion based models is infinite.



Annalen der Physik. **19** (1906), 371-381.

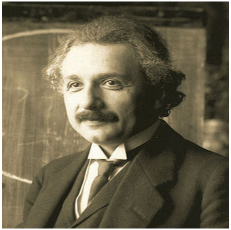
The solution for the Cauchy problem associated to equation (3) with initial data u_0 is given by

$$u(t,\cdot) = G_t \star u_0,$$

where G_t is the Gaussian

$$G_t(x) = (4\pi\nu t)^{-\frac{N}{2}} e^{-\frac{|x|}{4\nu t}}.$$

Starting with u_0 positive with compact support, $u(t,\cdot)$ becomes positive in all $\mathbb{R}^N$ for any time $t > 0$.
The propagation speed for classical linear diffusion based models is infinite.



Annalen der Physik. **19** (1906), 371-381.

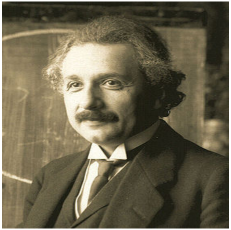
The solution for the Cauchy problem associated to equation (3) with initial data u_0 is given by

$$u(t, \cdot) = G_t \star u_0,$$

where G_t is the Gaussian

$$G_t(x) = (4\pi\nu t)^{-\frac{N}{2}} e^{-\frac{|x|}{4\nu t}}.$$

Starting with u_0 positive with compact support, $u(t, \cdot)$ becomes positive in all $\mathbb{R}^N$ for any time $t > 0$.
The propagation speed for classical linear diffusion based models is infinite.



Annalen der Physik. **19** (1906), 371-381.

P. Rosenau in 1992 proposed the following equation to correct the infinite speed of propagation of the linear diffusion theory

$$u_t = \nu \Delta u \;\Leftrightarrow\; u_t + \operatorname{div}(u V_u) = 0,$$

where the velocity V_u is given by

$$(a) \qquad V_u = -\nu \frac{\nabla u}{u}.$$

According to that if $|\frac{\nabla u}{u}| \uparrow \infty$ so will V_u.

Inertial imposes a macroscopic upper bound on the allowed free speed, namely, the speed of light c, or the acoustic speed C.

Rosenau modifies (a) as follows:

$$V_u = -\nu \frac{\nabla u}{\sqrt{u^2 + \frac{\nu^2}{c^2}|\nabla u|^2}}.$$

P. Rosenau in 1992 proposed the following equation to correct the infinite speed of propagation of the linear diffusion theory

$$u_t = \nu \Delta u \ \Leftrightarrow \ u_t + \operatorname{div}(u V_u) = 0,$$

where the velocity V_u is given by

$$(a) \qquad V_u = -\nu \frac{\nabla u}{u}.$$

According to that if $\left|\frac{\nabla u}{u}\right| \uparrow \infty$ so will V_u.

Inertial imposes a macroscopic upper bound on the allowed free speed, namely, the speed of light c, or the acoustic speed C.

Rosenau modifies (a) as follows:

$$V_u = -\nu \frac{\nabla u}{\sqrt{u^2 + \frac{\nu^2}{c^2}|\nabla u|^2}}.$$

P. Rosenau in 1992 proposed the following equation to correct the infinite speed of propagation of the linear diffusion theory

$$u_t = \nu \Delta u \ \Leftrightarrow \ u_t + \operatorname{div}(u V_u) = 0,$$

where the velocity V_u is given by

$$(a) \qquad V_u = -\nu \frac{\nabla u}{u}.$$

According to that if $|\frac{\nabla u}{u}| \uparrow \infty$ so will V_u.

Inertial imposes a macroscopic upper bound on the allowed free speed, namely, the speed of light c, or the acoustic speed C.

Rosenau modifies (a) as follows:

$$V_u = -\nu \frac{\nabla u}{\sqrt{u^2 + \frac{\nu^2}{c^2}|\nabla u|^2}}.$$

P. Rosenau in 1992 proposed the following equation to correct the infinite speed of propagation of the linear diffusion theory

$$u_t = \nu \Delta u \;\Leftrightarrow\; u_t + \operatorname{div}(u V_u) = 0,$$

where the velocity V_u is given by

$$(a) \qquad V_u = -\nu \frac{\nabla u}{u}.$$

According to that if $|\frac{\nabla u}{u}| \uparrow \infty$ so will V_u.

Inertial imposes a macroscopic upper bound on the allowed free speed, namely, the speed of light c, or the acoustic speed C.

Rosenau modifies (a) as follows:

$$V_u = -\nu \frac{\nabla u}{\sqrt{u^2 + \frac{\nu^2}{c^2}|\nabla u|^2}}.$$

P. Rosenau in 1992 proposed the following equation to correct the infinite speed of propagation of the linear diffusion theory

$$u_t = \nu \Delta u \iff u_t + \operatorname{div}(u V_u) = 0,$$

where the velocity V_u is given by

$$(a) \qquad V_u = -\nu \frac{\nabla u}{u}.$$

According to that if $|\frac{\nabla u}{u}| \uparrow \infty$ so will V_u.

Inertial imposes a macroscopic upper bound on the allowed free speed, namely, the speed of light c, or the acoustic speed C.

Rosenau modifies (a) as follows:

$$V_u = -\nu \frac{\nabla u}{\sqrt{u^2 + \frac{\nu^2}{c^2} |\nabla u|^2}}.$$

(*RHE*)
$$u_t = \nu \operatorname{div}\left(\frac{uDu}{\sqrt{u^2 + \frac{\nu^2}{c^2}|Du|^2}}\right),$$

where ν is a constant representing a kinematic viscosity and c the threshold speed of the problem (for instance the speed of light).

Equation (RHE) was derived by Y. Brenier (2001) by means of Monge-Kantorovich's mass transport theory and he named it as the relativistic heat equation

Brenier derived this equation as a gradient flow of the Boltzmann entropy for the metric corresponding to the cost function

$$k(z) := \begin{cases} c^2\left(1 - \sqrt{1 - \frac{|z|^2}{c^2}}\right) & \text{if } |z| \leq c \\ +\infty & \text{if } |z| > c. \end{cases}$$

$$(RHE) \qquad u_t = \nu \, \mathrm{div} \left(\frac{uDu}{\sqrt{u^2 + \frac{\nu^2}{c^2}|Du|^2}} \right),$$

where ν is a constant representing a kinematic viscosity and c the threshold speed of the problem (for instance the speed of light).

Equation (RHE) was derived by Y. Brenier (2001) by means of Monge-Kantorovich's mass transport theory and he named it as the relativistic heat equation

Brenier derived this equation as a gradient flow of the Boltzmann entropy for the metric corresponding to the cost function

$$k(z) := \begin{cases} c^2 \left(1 - \sqrt{1 - \frac{|z|^2}{c^2}} \right) & \text{if } \ |z| \le c \\ +\infty & \text{if } \ |z| > c. \end{cases}$$

(RHE) $$u_t = \nu \,\mathrm{div} \left(\frac{uDu}{\sqrt{u^2 + \frac{\nu^2}{c^2}|Du|^2}} \right),$$

where ν is a constant representing a kinematic viscosity and c the threshold speed of the problem (for instance the speed of light).

Equation (RHE) was derived by Y. Brenier (2001) by means of Monge-Kantorovich's mass transport theory and he named it as the relativistic heat equation

Brenier derived this equation as a gradient flow of the Boltzmann entropy for the metric corresponding to the cost function

$$k(z) := \begin{cases} c^2 \left(1 - \sqrt{1 - \frac{|z|^2}{c^2}} \right) & \text{if} \quad |z| \leq c \\ +\infty & \text{if} \quad |z| > c. \end{cases}$$

In [F. ANDREU, V. CASELLES & J.M. MAZÓN. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.] we have proved existence and uniqueness of entropy solutions for the Cauchy problem for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \operatorname{div} \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0,T) \times \mathbb{R}^N \\ u(0,x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases} \tag{4}$$

$\mathbf{a}(z,\xi) = \nabla_\xi f(z,\xi)$ and f being a function with linear growth as $\|\xi\| \to \infty$, satisfying some assumptions.

- relativistic heat equation
- flux limiter equation of Wilson $\quad u_t = \nu \operatorname{div}\left(\dfrac{uDu}{u + \frac{\nu}{c}|Du|}\right)$
- plasma equation $\quad \dfrac{\partial u}{\partial t} = \left(\dfrac{u^{5/2}u_x}{1+u|u_x|}\right)_x,$

In [F. ANDREU, V. CASELLES & J.M. MAZÓN. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.] we have proved existence and uniqueness of entropy solutions for the Cauchy problem for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \operatorname{div} \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0, T) \times \mathbb{R}^N \\ u(0, x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases} \tag{4}$$

$\mathbf{a}(z, \xi) = \nabla_\xi f(z, \xi)$ and f being a function with linear growth as $\|\xi\| \to \infty$, satisfying some assumptions.

- relativistic heat equation
- flux limiter equation of Wilson $\quad u_t = \nu \operatorname{div} \left(\dfrac{uDu}{u + \frac{\nu}{c}|Du|} \right)$
- plasma equation $\quad \dfrac{\partial u}{\partial t} = \left(\dfrac{u^{5/2} u_x}{1 + u|u_x|} \right)_x,$

Difficulties and problems

1. Due to the linear growth, the natural energy space is the space $BV(\mathbb{R}^N)$ of functions of bounded variation.

2. Due to the lack of coercivity, we need to consider the following truncature functions. For $a < b$, let $T_{a,b}(r) := \max(\min(b, r), a)$.

3. We need to consider the function space

$$TBV^+(\mathbb{R}^N) := \{u \in L^1(\mathbb{R}^N)^+ \ : \ T_{a,b}(u) \in BV(\mathbb{R}^N), \ \forall\, 0 < a < b\},$$

   and to give a sense to the Radon-Nikodym derivative (with respect to the Lebesgue measure) ∇u of Du for a function $u \in TBV^+(\mathbb{R}^N)$.

4. In this framework we give sense the the differential operator

$$\mathrm{div}\ \mathbf{a}(u, Du)$$

5. We prove existence and uniqueness of entropy solution for the problem

$$u + \lambda \mathrm{div}\ \mathbf{a}(u, Du) = f \quad \text{for any } f \in L^1(\mathbb{R}^N), \ \lambda > 0.$$

Difficulties and problems

1. Due to the linear growth, the natural energy space is the space $BV(\mathbb{R}^N)$ of functions of bounded variation.
2. Due to the lack of coercivity, we need to consider the following truncature functions. For $a < b$, let $T_{a,b}(r) := \max(\min(b,r),a)$.
3. We need to consider the function space

$$TBV^+(\mathbb{R}^N) := \{u \in L^1(\mathbb{R}^N)^+ \ : \ T_{a,b}(u) \in BV(\mathbb{R}^N), \ \forall\, 0 < a < b\},$$

   and to give a sense to the Radon-Nikodym derivative (with respect to the Lebesgue measure) ∇u of Du for a function $u \in TBV^+(\mathbb{R}^N)$.
4. In this framework we give sense the the differential operator

$$\mathrm{div}\, \mathbf{a}(u, Du)$$

5. We prove existence and uniqueness of entropy solution for the problem

$$u + \lambda \mathrm{div}\, \mathbf{a}(u, Du) = f \quad \text{for any } f \in L^1(\mathbb{R}^N), \ \lambda > 0.$$

Difficulties and problems

1. Due to the linear growth, the natural energy space is the space $BV(\mathbb{R}^N)$ of functions of bounded variation.

2. Due to the lack of coercivity, we need to consider the following truncature functions. For $a < b$, let $T_{a,b}(r) := \max(\min(b, r), a)$.

3. We need to consider the function space

$$TBV^+(\mathbb{R}^N) := \{u \in L^1(\mathbb{R}^N)^+ \ : \ T_{a,b}(u) \in BV(\mathbb{R}^N), \ \forall\, 0 < a < b\},$$

and to give a sense to the Radon-Nikodym derivative (with respect to the Lebesgue measure) ∇u of Du for a function $u \in TBV^+(\mathbb{R}^N)$.

4. In this framework we give sense the the differential operator

$$\mathrm{div}\ \mathbf{a}(u, Du)$$

5. We prove existence and uniqueness of entropy solution for the problem

$$u + \lambda \mathrm{div}\ \mathbf{a}(u, Du) = f \quad \text{for any } f \in L^1(\mathbb{R}^N), \ \lambda > 0.$$

Difficulties and problems

1. Due to the linear growth, the natural energy space is the space $BV(\mathbb{R}^N)$ of functions of bounded variation.
2. Due to the lack of coercivity, we need to consider the following truncature functions. For $a < b$, let $T_{a,b}(r) := \max(\min(b, r), a)$.
3. We need to consider the function space

   $$TBV^+(\mathbb{R}^N) := \left\{ u \in L^1(\mathbb{R}^N)^+ \ : \ T_{a,b}(u) \in BV(\mathbb{R}^N), \ \ \forall\, 0 < a < b \right\},$$

   and to give a sense to the Radon-Nikodym derivative (with respect to the Lebesgue measure) ∇u of Du for a function $u \in TBV^+(\mathbb{R}^N)$.
4. In this framework we give sense the the differential operator

   $$\mathrm{div}\ \mathbf{a}(u, Du)$$

5. We prove existence and uniqueness of entropy solution for the problem

   $$u + \lambda \mathrm{div}\ \mathbf{a}(u, Du) = f \quad \text{for any } f \in L^1(\mathbb{R}^N), \ \lambda > 0.$$

Difficulties and problems

1. Due to the linear growth, the natural energy space is the space $BV(\mathbb{R}^N)$ of functions of bounded variation.
2. Due to the lack of coercivity, we need to consider the following truncature functions. For $a < b$, let $T_{a,b}(r) := \max(\min(b, r), a)$.
3. We need to consider the function space

$$TBV^+(\mathbb{R}^N) := \{u \in L^1(\mathbb{R}^N)^+ \ : \ T_{a,b}(u) \in BV(\mathbb{R}^N), \ \forall\, 0 < a < b\},$$

   and to give a sense to the Radon-Nikodym derivative (with respect to the Lebesgue measure) ∇u of Du for a function $u \in TBV^+(\mathbb{R}^N)$.
4. In this framework we give sense the the differential operator

$$\mathrm{div}\ \mathbf{a}(u, Du)$$

5. We prove existence and uniqueness of entropy solution for the problem

$$u + \lambda \mathrm{div}\ \mathbf{a}(u, Du) = f \quad \text{for any } f \in L^1(\mathbb{R}^N), \ \lambda > 0.$$

Difficulties and problems

1. Due to the linear growth, the natural energy space is the space $BV(\mathbb{R}^N)$ of functions of bounded variation.
2. Due to the lack of coercivity, we need to consider the following truncature functions. For $a < b$, let $T_{a,b}(r) := \max(\min(b, r), a)$.
3. We need to consider the function space

$$TBV^+(\mathbb{R}^N) := \left\{u \in L^1(\mathbb{R}^N)^+ \ : \ T_{a,b}(u) \in BV(\mathbb{R}^N), \ \forall\, 0 < a < b\right\},$$

   and to give a sense to the Radon-Nikodym derivative (with respect to the Lebesgue measure) ∇u of Du for a function $u \in TBV^+(\mathbb{R}^N)$.
4. In this framework we give sense the the differential operator

$$\mathrm{div}\ \mathbf{a}(u, Du)$$

5. We prove existence and uniqueness of entropy solution for the problem

$$u + \lambda \mathrm{div}\ \mathbf{a}(u, Du) = f \quad \text{for any } f \in L^1(\mathbb{R}^N), \ \lambda > 0.$$

1. Applying Crandall-Liggett's Theorem we obtain the existence and uniqueness of mild-solution of the corresponding abstract Cauchy problem

2. We introduce the concept of entropy solution for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \operatorname{div} \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0, T) \times \mathbb{R}^N \\ u(0, x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases}$$

3. We prove uniqueness of entropy solutions (by Kruzkov's method of doubling variables)

4. We show that entropy solutions and mild solutions coincides.

5. One difficulty is that, in general, the time derivative u_t is not an integrable function, it is a Radon measure

1. Applying Crandall-Liggett's Theorem we obtain the existence and uniqueness of mild-solution of the corresponding abstract Cauchy problem
2. We introduce the concept of entropy solution for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \operatorname{div} \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0, T) \times \mathbb{R}^N \\ u(0, x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases}$$

3. We prove uniqueness of entropy solutions (by Kruzkov's method of doubling variables)
4. We show that entropy solutions and mild solutions coincides.
5. One difficulty is that, in general, the time derivative u_t is not an integrable function, it is a Radon measure

1. Applying Crandall-Liggett's Theorem we obtain the existence and uniqueness of mild-solution of the corresponding abstract Cauchy problem
2. We introduce the concept of entropy solution for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \mathrm{div}\, \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0, T) \times \mathbb{R}^N \\ u(0,x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases}$$

3. We prove uniqueness of entropy solutions (by Kruzkov's method of doubling variables)
4. We show that entropy solutions and mild solutions coincides.
5. One difficulty is that, in general, the time derivative u_t is not an integrable function, it is a Radon measure

1. Applying Crandall-Liggett's Theorem we obtain the existence and uniqueness of mild-solution of the corresponding abstract Cauchy problem

2. We introduce the concept of entropy solution for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \mathrm{div}\, \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0, T) \times \mathbb{R}^N \\ u(0, x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases}$$

3. We prove uniqueness of entropy solutions (by Kruzkov's method of doubling variables)

4. We show that entropy solutions and mild solutions coincides.

5. One difficulty is that, in general, the time derivative u_t is not an integrable function, it is a Radon measure

1. Applying Crandall-Liggett's Theorem we obtain the existence and uniqueness of mild-solution of the corresponding abstract Cauchy problem

2. We introduce the concept of entropy solution for the quasi-linear parabolic equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = \operatorname{div} \mathbf{a}(u, Du) & \text{in} \quad Q_T = (0, T) \times \mathbb{R}^N \\[2ex] u(0, x) = u_0(x) & \text{in} \quad x \in \mathbb{R}^N \end{cases}$$

3. We prove uniqueness of entropy solutions (by Kruzkov's method of doubling variables)

4. We show that entropy solutions and mild solutions coincides.

5. One difficulty is that, in general, the time derivative u_t is not an integrable function, it is a Radon measure

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

References on the flux-limitation theory

F. Andreu, V. Caselles and J. M. Mazón. The Cauchy Problem for a Strong Degenerate Quasilinear Equation. J. Europ. Math. Soc. **7** (2005), 361-393.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. Finite Propagation Speed for Limited Flux Diffusion Equations. Arch. Rat. Mech. Anal. 182 (2006), no. 2, 269–297.

F. Andreu, V. Caselles and J. M. Mazón. Some regularity results on the relativistic heat equation J. Differential Equations 245 (2008) 3639-3663.

F. Andreu, V. Caselles and J. M. Mazón. A Fisher-Kolmogorov equation with finite speed of propagation, J. Differential Equations **248** (2010) 2528-2561.

F. Andreu, V. Caselles and J. M. Mazón & S. Moll. The Dirichlet problem associated to the relativistic heat equation.. Math. Ann. 347 (2010), no. 1, 135-199.

V. Caselles, On the entropy conditions for some flux limited diffusion equations, J. Diff. Eq. **250** (2011), 3311-3348.

F. Andreu, V. Caselles, J.M. Mazón, J. Soler and M. Verbeni. Radially Symmetric Solutions of a Tempered Diffusion Equation. A porous media–flux–limited case. SIAM J. Math. Anal. **44** (2012), 1019-1049.

Modification of the model

- Change the equation describing transport of morphogen in neural tube: introduction of a flux limiter

$$\frac{\partial[\mathrm{Shh}]}{\partial t} = \nu\,\partial_x \frac{[\mathrm{Shh}]\partial_x[\mathrm{Shh}]}{\sqrt{[\mathrm{Shh}]^2 + \frac{\nu^2}{c^2}(\partial_x[\mathrm{Shh}])^2}}$$

$$+ k_{off}[\mathrm{Ptc1Shh}_{out}] - k_{on}[\mathrm{Shh}][\mathrm{Ptc1}_{out}]$$

(M. Verbeni, O. Sánchez, E. Mollica, I. Guerrero, A. Ruiz i Altaba, Juan Soler)

Reaction–diffusion

$$\frac{\partial[\mathrm{Shh}]}{\partial t} = \nu\,\partial_x \frac{[\mathrm{Shh}]\partial_x[\mathrm{Shh}]}{\sqrt{[\mathrm{Shh}]^2 + \frac{\nu^2}{c^2}(\partial_x[\mathrm{Shh}])^2}} + k_{off}[\mathrm{Ptc1Shh}_{out}] - k_{on}[\mathrm{Shh}][\mathrm{Ptc1}_{out}]$$

Biochemical reactions in the cell

$$\begin{aligned}
\frac{\partial}{\partial t}[\mathrm{Ptc1Shh}_{out}] &= -(k_{off}+k_{Cin})[\mathrm{Ptc1Shh}_{out}] + k_{on}[\mathrm{Shh}][\mathrm{Ptc1}_{out}] + k_{Cout}[\mathrm{Ptc1Shh}_{in}]\\
\frac{\partial}{\partial t}[\mathrm{Ptc1Shh}_{in}] &= k_{Cin}[\mathrm{Ptc1Shh}_{out}] - k_{Cout}[\mathrm{Ptc1Shh}_{in}] - k_{Cdeg}[\mathrm{Ptc1Shh}_{in}]\\
\frac{\partial}{\partial t}[\mathrm{Ptc1}_{out}] &= k_{off}[\mathrm{Ptc1Shh}_{out}] - k_{on}[\mathrm{Shh}][\mathrm{Ptc1}_{out}] + k_{Pint}[\mathrm{Ptc1_{int}}]\\
\frac{\partial}{\partial t}[\mathrm{Ptc1_{int}}] &= k_P\,P_{tr}\,\{[\mathrm{Gli1A}](\mathrm{t}-\tau),[\mathrm{Gli3A}](\mathrm{t}),[\mathrm{Gli3R}](\mathrm{t})\}\;Y_{\mathrm{Ptc}} - k_{Pint}[\mathrm{Ptc1_{int}}],\quad \mathrm{Y_{Ptc}} = \frac{\mathrm{K_{Ptc}}}{[\mathrm{Ptc1_{out}}]+\mathrm{K_{Ptc}}}\\
\frac{\partial}{\partial t}[\mathrm{Gli1A}] &= k_G\,P_{tr}\,\{[\mathrm{Gli1A}](\mathrm{t}-\tau),[\mathrm{Gli3A}](\mathrm{t}),[\mathrm{Gli3R}](\mathrm{t})\}\;Y_{\mathrm{Ptc}} - k_{deg}[\mathrm{Gli1A}]\\
\frac{\partial}{\partial t}[\mathrm{Gli3R}] &= [\mathrm{Gli3A}]\frac{\mathrm{k_{g3r}}}{1+\mathrm{R_{Ptc}}} - \mathrm{k_{deg}}[\mathrm{Gli3R}], \qquad \mathrm{R_{Ptc}} = \frac{[\mathrm{Ptc1Shh_{out}}]}{[\mathrm{Ptc1_{out}}]}\\
\frac{\partial}{\partial t}[\mathrm{Gli3A}] &= \frac{\gamma_{g3}}{1+R_{Ptc}} - [\mathrm{Gli3A}]\frac{\mathrm{k_{g3r}}}{1+\mathrm{R_{Ptc}}} - \mathrm{k_{deg}}[\mathrm{Gli3A}]
\end{aligned}$$

A model for the transport of morphogenes

$$\begin{cases} \dfrac{\partial u}{\partial t} = (\mathbf{a}(u, u_x))_x - f(t-\tau, u(t,x))\, u(t,x) + g(t, u(t,x)), & \text{in } \;]0,T[\times]0,L \\ -\mathbf{a}(u(t,0), u_x(t,0)) = \beta > 0 \;\text{ and }\; u(t,L) = 0 & \text{in } \; t \in]0,T[, \\ u(0,x) = u_0(x) & \text{in } \; x \in]0,L[, \end{cases} \tag{5}$$

where

$$\mathbf{a}(z,\xi) := \nu \frac{|z|\xi}{\sqrt{z^2 + \frac{\nu^2}{c^2}|\xi|^2}},$$

F. Andreu, J. Calvo, J. M. Mazón and J. Soler. On a nonlinear flux–limited equation arising in the transport of morphogens. J. Diff. Equat. **252** (2012), 5763-5813.

A model for the transport of morphogenes

$$
\begin{cases}
\dfrac{\partial u}{\partial t} = (\mathbf{a}(u,u_x))_x - f(t-\tau, u(t,x))\, u(t,x) + g(t, u(t,x)), & \text{in } \;]0,T[\times]0,L \\
-\mathbf{a}(u(t,0), u_x(t,0)) = \beta > 0 \;\text{ and }\; u(t,L) = 0 & \text{in } \; t \in]0,T[, \\
u(0,x) = u_0(x) & \text{in } \; x \in]0,L[,
\end{cases}
\tag{5}
$$

where

$$
\mathbf{a}(z,\xi) := \nu \frac{|z|\xi}{\sqrt{z^2 + \frac{\nu^2}{c^2}|\xi|^2}},
$$

F. Andreu, J. Calvo, J. M. Mazón and J. Soler. On a nonlinear flux–limited equation arising in the transport of morphogens. J. Diff. Equat. **252** (2012), 5763-5813.

Transport of morphogens

$$\begin{cases} \dfrac{\partial u}{\partial t} = \nu \left(\dfrac{u u_x}{\sqrt{u^2 + \frac{\nu^2}{c^2} u_x^2}} \right)_x, & \text{in} \quad]0, T[\times]0, L[, \\ -\mathbf{a}(u(t,0), u_x(t,0)) = \beta > 0 \ \text{ and } \ u(t, L) = 0, & \text{in} \quad t \in]0, T[, \\ u(0, x) = u_0(x), & \text{in} \quad x \in]0, L[, \end{cases} \tag{6}$$

Theorem

For every initial datum $0 \leq u_0 \in L^\infty(]0, L[)$, there is a unique entropy bounded solution u of the problem (6) in $Q_T =]0, T[\times]0, L[$ for any $T > 0$ such that $u(0) = u_0$.

Transport of morphogens

$$
\begin{cases}
\dfrac{\partial u}{\partial t} = \nu \left(\dfrac{u u_x}{\sqrt{u^2 + \frac{\nu^2}{c^2} u_x^2}} \right)_x, & \text{in} \quad]0,T[\times]0,L[, \\[2ex]
-\mathbf{a}(u(t,0), u_x(t,0)) = \beta > 0 \ \ \text{and} \ \ u(t,L) = 0, & \text{in} \quad t \in]0,T[, \\[2ex]
u(0,x) = u_0(x), & \text{in} \quad x \in]0,L[,
\end{cases}
\tag{6}
$$

Theorem

For every initial datum $0 \leq u_0 \in L^\infty(]0,L[)$, there is a unique entropy bounded solution u of the problem (6) in $Q_T =]0,T[\times]0,L[$ for any $T > 0$ such that $u(0) = u_0$.

$$
\begin{cases} -\left(\mathbf{a}(u,u')\right)' = v & \text{in} \quad]0,L[\\ \\ -\mathbf{a}(u,u')|_{x=0} = \beta > 0 \quad \text{and} \quad u(L) = 0, \end{cases} \tag{7}
$$

where $v \in L^1(]0,L[)$.

Tools

- Generalized Green's Formula (Anzellotti)
- The Kruzkov method doublin variables .
- A Functionl Calculus inspired in the relax energy functional, for linear growth functional introduced by Dal Maso

$$\begin{cases} -(\mathbf{a}(u,u'))' = v & \text{in } \;]0,L[\\ -\mathbf{a}(u,u')|_{x=0} = \beta > 0 \;\text{ and }\; u(L) = 0, & \end{cases} \tag{7}$$

where $v \in L^1(]0,L[)$.

Tools

- Generalized Green's Formula (Anzellotti)
- The Kruzkov method doublin variables .
- A Functionl Calculus inspired in the relax energy functional, for linear growth functional introduced by Dal Maso

$$
\begin{cases} -\left(\mathbf{a}(u,u')\right)' = v & \text{in} \quad]0,L[\\ \\ -\mathbf{a}(u,u')|_{x=0} = \beta > 0 \quad \text{and} \quad u(L) = 0, \end{cases} \tag{7}
$$

where $v \in L^1(]0,L[)$.

Tools

- Generalized Green's Formula (Anzellotti)
- The Kruzkov method doublin variables .
- A Functionl Calculus inspired in the relax energy functional, for linear growth functional introduced by Dal Maso

Theorem

For any $0 \leq f \in L^\infty(]0,L[)$ *there exists a unique entropy solution* $u \in TBV^+(]0,L[)$ *of the problem*

$$\begin{cases} u - (\mathbf{a}(u,u'))' = f & \text{in }]0,L[\\ -\mathbf{a}(u,u')|_{x=0} = \beta > 0 & u(L) = 0, \end{cases} \tag{8}$$

which satisfies $||u||_\infty \leq M(\beta, c, \nu, ||f||_\infty)$.
Moreover, let $u, \overline{u}$ *be two entropy solutions of (8) associated to* $f, \overline{f} \in L^1(]0,L[)^+$, *respectively. Then,*

$$\int_0^L (u - \overline{u})^+ \, dx \leq \int_0^L (f - \overline{f})^+ \, dx.$$

We associate an accretive operator in $L^1(]0,L[)$ to the problem (7).

Definition

$(u,v) \in \mathcal{B}_\beta$ if and only if $0 \leq u \in TBV^+(]0,L[)$, $v \in L^1(]0,L[)$ and u is the entropy solution of problem (7).

Theorem

For any $0 \leq f \in L^\infty(]0,L[)$ *there exists a unique entropy solution* $u \in TBV^+(]0,L[)$ *of the problem*

$$\begin{cases} u - (\mathbf{a}(u,u'))' = f & \text{in }]0,L[\\ -\mathbf{a}(u,u')|_{x=0} = \beta > 0 & u(L) = 0, \end{cases} \tag{8}$$

which satisfies $||u||_\infty \leq M(\beta, c, \nu, ||f||_\infty)$.
Moreover, let $u, \overline{u}$ *be two entropy solutions of (8) associated to* $f, \overline{f} \in L^1(]0,L[)^+$, *respectively. Then,*

$$\int_0^L (u - \overline{u})^+ \, dx \leq \int_0^L (f - \overline{f})^+ \, dx.$$

We associate an accretive operator in $L^1(]0,L[)$ to the problem (7).

Definition

$(u,v) \in \mathcal{B}_\beta$ if and only if $0 \leq u \in TBV^+(]0,L[)$, $v \in L^1(]0,L[)$ and u is the entropy solution of problem (7).

From the above Theorem, it follows that the operator $\mathcal{B}_\beta$ is T-accretive in $L^1(]0,L[)$ and verifies

$$L^\infty(]0,L[)^+ \subset R(I+\lambda\mathcal{B}_\beta) \quad \text{for all} \quad \lambda > 0. \tag{9}$$

Then, according to Crandall-Liggett's Theorem, for any $0 \leq u_0 \in L^1(]0,L[)$ there exists a unique mild solution $u \in C([0,T];L^1(]0,L[))$ of the abstract Cauchy problem

$$u'(t) + \mathcal{B}_\beta u(t) \ni 0, \qquad u(0) = u_0.$$

Moreover, $u(t) = T_\beta(t)u_0$ for all $t \geq 0$, where $(T_\beta(t))_{t\geq 0}$ is the semigroup in $L^1(]0,L[)^+$ generated by Crandall-Liggett's exponential formula, i.e.,

$$T_\beta(t)u_0 = \lim_{n\to\infty}\left(I + \frac{t}{n}\mathcal{B}_\beta\right)^{-n} u_0.$$

From the above Theorem, it follows that the operator $\mathcal{B}_\beta$ is T-accretive in $L^1(]0,L[)$ and verifies

$$L^\infty(]0,L[)^+ \subset R(I+\lambda\mathcal{B}_\beta) \quad \text{for all} \quad \lambda > 0. \tag{9}$$

Then, according to Crandall-Liggett's Theorem, for any $0 \leq u_0 \in L^1(]0,L[)$ there exists a unique mild solution $u \in C([0,T];L^1(]0,L[))$ of the abstract Cauchy problem

$$u'(t) + \mathcal{B}_\beta u(t) \ni 0, \qquad u(0) = u_0.$$

Moreover, $u(t) = T_\beta(t)u_0$ for all $t \geq 0$, where $(T_\beta(t))_{t\geq 0}$ is the semigroup in $L^1(]0,L[)^+$ generated by Crandall-Liggett's exponential formula, i.e.,

$$T_\beta(t)u_0 = \lim_{n\to\infty}\left(I + \frac{t}{n}\mathcal{B}_\beta\right)^{-n} u_0.$$

J. Calvo, J. M. Mazón, J. Soler and M. Verbeni. Qualitative properties of the solutions of a nonlinear flux–limited equation arising in the transport of morphogens. M3AS **21** (2011), 893-937.

Theorem

We have that

$$supp(U_0(t)) =]0, ct[\quad for \ \ 0 < t \leq \frac{L}{c},$$

being $U_0(t)$ the entropy solution of the problem (6) such that $U_0(0) = 0$.

Comparison principle between soluion and sub and super solution

Explicit sub and super solutions

J. Calvo, J. M. Mazón, J. Soler and M. Verbeni. Qualitative properties of the solutions of a nonlinear flux–limited equation arising in the transport of morphogens. M3AS **21** (2011), 893-937.

Theorem

We have that

$$supp(U_0(t)) =]0, ct[\quad for \;\; 0 < t \leq \frac{L}{c},$$

being $U_0(t)$ the entropy solution of the problem (6) such that $U_0(0) = 0$.

Comparison principle between soluion and sub and super solution

Explicit sub and super solutions

J. Calvo, J. M. Mazón, J. Soler and M. Verbeni. Qualitative properties of the solutions of a nonlinear flux–limited equation arising in the transport of morphogens. M3AS **21** (2011), 893-937.

Theorem

We have that

$$supp(U_0(t)) =]0, ct[\quad \textit{for} \;\; 0 < t \leq \frac{L}{c},$$

being $U_0(t)$ the entropy solution of the problem (6) such that $U_0(0) = 0$.

Comparison principle between soluion and sub and super solution

Explicit sub and super solutions

Proposition

There are values $0 \leq a < L$, $c_2 > 0$ *and* $\mu > 1$ *such that*

$$u(t,x) = \left(\mu \frac{\beta}{c} + c_2 t - \frac{\beta}{\nu} \frac{\mu}{\sqrt{\mu^2 - 1}} x \right) \chi_{]0,a+ct[}(x)$$

is a supersolution of the problem (6) in the time interval $[0,(L-a)/c]$ *and with initial datum*

$$u_0(x) = \left(\mu \frac{\beta}{c} - \frac{\beta}{\nu} \frac{\mu}{\sqrt{\mu^2 - 1}} x \right) \chi_{]0,a[}(x).$$

Proposition

The function

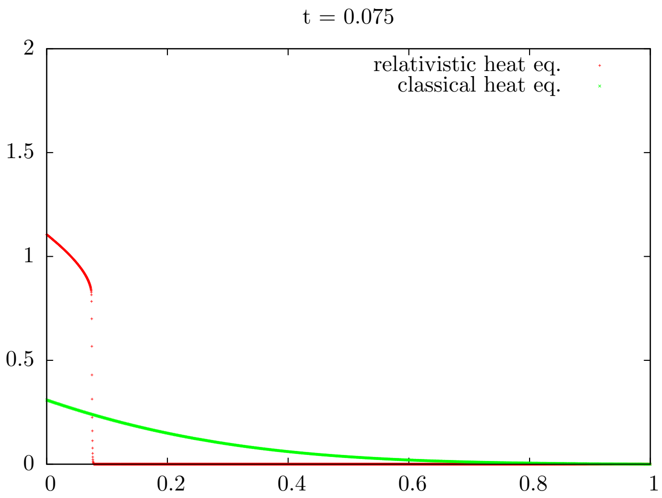
$$W(t,x) := \left(\frac{\beta}{c} + \varphi(t)x\right)\chi_{]0,\min\{ct,L\}[}(x) \tag{10}$$

is a sub-solution of the problem (6) with zero initial datum, where $\varphi(t) = -\frac{\beta}{c^2 t}$ *for* $0 < t \leq \frac{L}{c}$ *and, for* $t > \frac{L}{c}$, $\varphi(t)$ *is given as the solution of*

$$\varphi'(t) = \frac{\nu^3}{c^2 L}\frac{\varphi(t)^4}{\left((\frac{\beta}{c} + L\varphi(t))^2 + \frac{\nu^2}{c^2}\varphi(t)^2\right)^{3/2}}$$

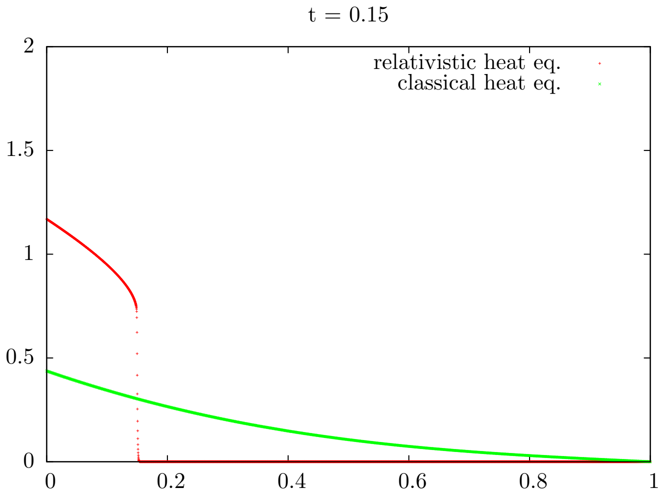
with $\varphi(L/c) = -\frac{\beta}{cL}$.

Numerical comparison



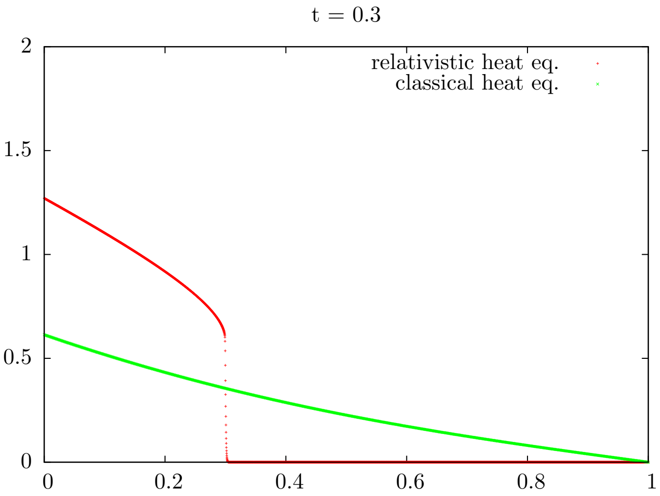
(Calvo, Mazón, Soler, Verbeni)

Numerical comparison



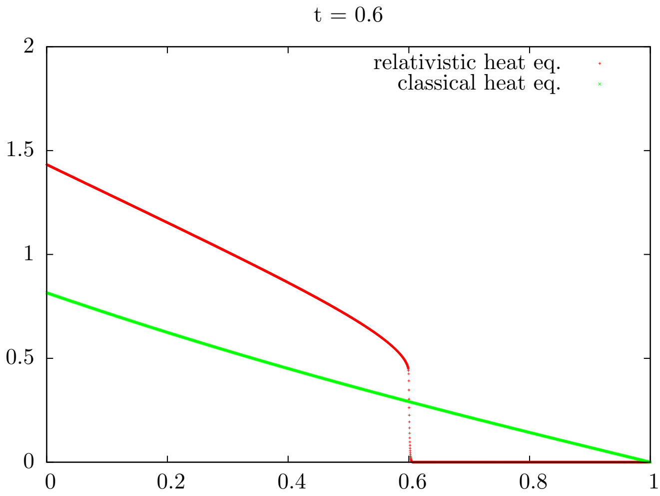
(Calvo, Mazón, Soler, Verbeni)

Numerical comparison



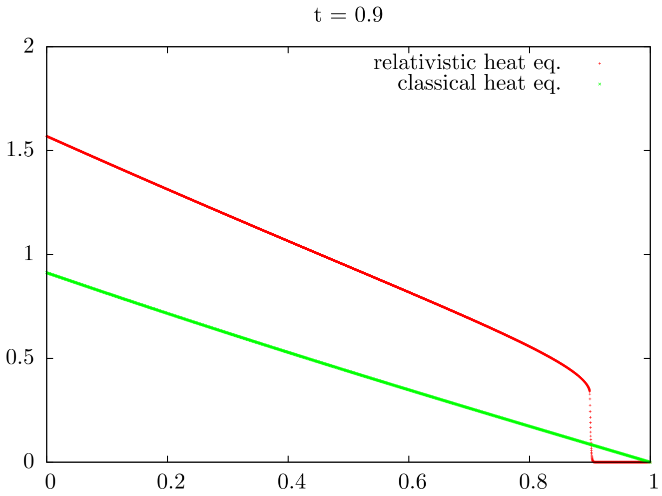
(Calvo, Mazón, Soler, Verbeni)

Numerical comparison



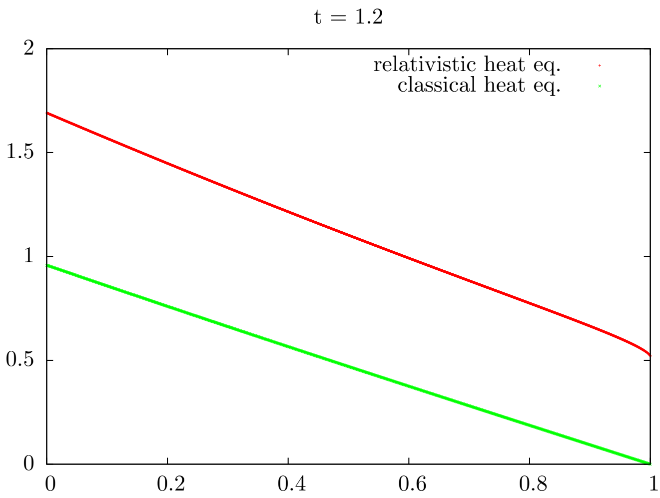
(Calvo, Mazón, Soler, Verbeni)

Numerical comparison



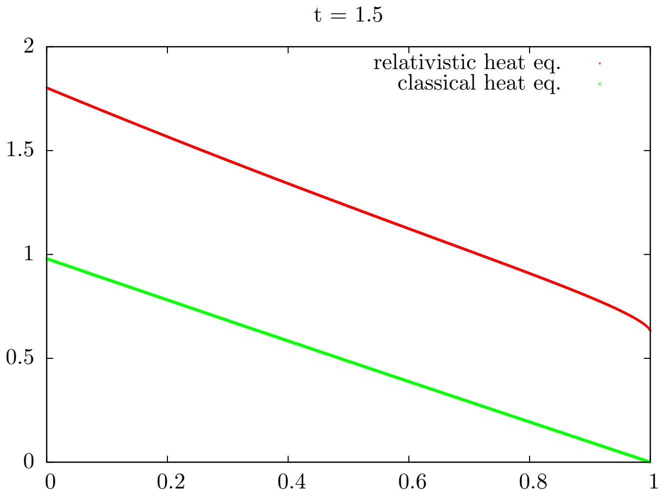
(Calvo, Mazón, Soler, Verbeni)

Numerical comparison



(Calvo, Mazón, Soler, Verbeni)

Numerical comparison



(Calvo, Mazón, Soler, Verbeni)

Theorem

There is a non-increasing function $u_\beta \in C^1(]0,L[)$, with $u_\beta \geq \frac{\beta}{c}$, that is the unique entropy solution of the stationary problem

$$\begin{cases} -\Big(\mathbf{a}(u_\beta, u_\beta')\Big)' = 0 & \text{in }]0,L[\\ -\mathbf{a}(u_\beta, u_\beta')|_{x=0} = \beta > 0 & \text{and } u_\beta(L) = 0 \end{cases} \tag{11}$$

Theorem

For every $u_0 \in L^\infty(]0,L[)^+$, we have that

$$\lim_{t \to +\infty} \| T_\beta(t) u_0 - u_\beta \|_1 = 0,$$

where $u(t) = T_\beta(t)u_0$ is the unique entropy solution of the problem (6) with initial datum u_0.

Theorem

There is a non-increasing function $u_\beta \in C^1(]0,L[)$, with $u_\beta \geq \frac{\beta}{c}$, that is the unique entropy solution of the stationary problem

$$\begin{cases} -\Big(\mathbf{a}(u_\beta, u'_\beta)\Big)' = 0 & \text{in }]0,L[\\ -\mathbf{a}(u_\beta, u'_\beta)|_{x=0} = \beta > 0 & \text{and } u_\beta(L) = 0 \end{cases} \tag{11}$$

Theorem

For every $u_0 \in L^\infty(]0,L[)^+$, we have that

$$\lim_{t\to+\infty} \| T_\beta(t)u_0 - u_\beta \|_1 = 0,$$

where $u(t) = T_\beta(t)u_0$ is the unique entropy solution of the problem (6) with initial datum u_0.