A Hyperbolic System of Chemotaxis on Network Modeling Physarum Dynamics

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Chemotaxis

Movements of individuals (bacteria, human cells,...) under the effect of changes of gradient of chemical substance – the chemoattractant.

Dictyostellium (dicty) discoideum, Physarum polycephalum, Angiogenesis, Stem cells, Fibroblasts.

Greenberg-Alt chemotaxis model on a line

Greenberg-Alt PDE model
(hyperbolic-parabolic)

$$\begin{cases} u_t + v_x = 0, \\ v_t + \lambda^2 u_x = \chi \phi_x\, u - v, \\ \phi_t - D\, \phi_{xx} = au - b\phi. \end{cases}$$

with boundary conditions:

- Neumann for u and ϕ;
- Dirichlet for v.

- u is the density of cells
- v is the averaged flux
- ϕ is the density of chemoattractant
- $\lambda > 0$ is the velocity of cells
- χ is the chemotactic sensitivity
- a,b production and degradation rates of ϕ
- D diffusion coefficient of ϕ

GA model on a line

$$\begin{cases} u_t + v_x = 0, \\ v_t + \lambda^2 u_x = \chi \phi_x \, u - v, \\ \phi_t - D \, \phi_{xx} = au - b\phi. \end{cases}$$
$\Longleftrightarrow$
$$\begin{cases} u_t^+ + \lambda u_x^+ = \dfrac{1}{2\lambda} \left((\chi \phi_x - \lambda) u^+ + (\chi \phi_x + \lambda) u^- \right), \\ u_t^- - \lambda u_x^- = -\dfrac{1}{2\lambda} \left((\chi \phi_x - \lambda) u^+ + (\chi \phi_x + \lambda) u^- \right), \\ \phi_t - D\phi_{xx} = a(u^+ + u^-) - b\phi. \end{cases}$$

Mass conservation:

$$\int_{[0,L]} u(x, t) \, dx = \int_{[0,L]} u(x, 0) \, dx.$$

$$\boxed{\begin{array}{ll} u = u^+ + u^- & \quad u^\pm = \dfrac{1}{2} \left(u \pm \dfrac{v}{\lambda} \right) \\ v = \lambda(u^+ - u^-) & \end{array}}$$

Diagonal variables: density of cells following the orientation of the line / density of cells going in the opposite direction

Theoretical results:
• 1D: existence of global in time solutions *[Guarguaglini, Mascia, Natalini, Ribot, 09]*
• multiD: existence of global solutions in time for small data *[DiRusso, Natalini, Ribot, 2010; DiRusso, 2016]*
• 2D: numerical evidences of blow-up phenomena for big data

Numerical scheme on a line [Natalini-Ribot12]

- **Hyperbolic part (second order AHO scheme):**

$$u_{-,i}^{n+1,j} = \left(1 - \lambda_i \frac{k}{h_i} - \frac{k}{4}\right) u_{-,i}^{n,j} + \left(\frac{k\lambda_i}{h_i} - \frac{k}{4}\right) u_{-,i}^{n,j+1} + \frac{k}{4}(u_{+,i}^{n,j} + u_{+,i}^{n,j+1})$$

$$- \frac{k}{4\lambda_i}\left(f_i^{n,j+1} + f_i^{n,j}\right), \quad j = 0, \ldots, M_i, i = 1, \ldots, N,$$

$$u_{+,i}^{n+1,j} = \left(1 - \lambda_i \frac{k}{h_i} - \frac{k}{4}\right) u_{+,i}^{n,j} + \left(\frac{k\lambda_i}{h_i} - \frac{k}{4}\right) u_{+,i}^{n,j-1} + \frac{k}{4}(u_{-,i}^{n,j} + u_{-,i}^{n,j-1})$$

$$+ \frac{k}{4\lambda_i}\left(f_i^{n,j-1} + f_i^{n,j}\right), \quad j = 1, \ldots, M_i + 1, i = 1, \ldots, N.$$

Monotonicity condition: $\quad h \leq 4\lambda$ and $k \leq \dfrac{4h}{h + 4\lambda}$,

$$f = \chi \phi_x u \qquad \text{Source term}$$

$$\phi_{x,i}^{n+1,j} = \frac{1}{2h_i}\left(\phi_i^{n+1,j+1} - \phi_i^{n+1,j-1}\right), 1 \leq j \leq M_i$$

See also Well-balanced [L. Gosse]

Numerical scheme on a line [Natalini-Ribot12]

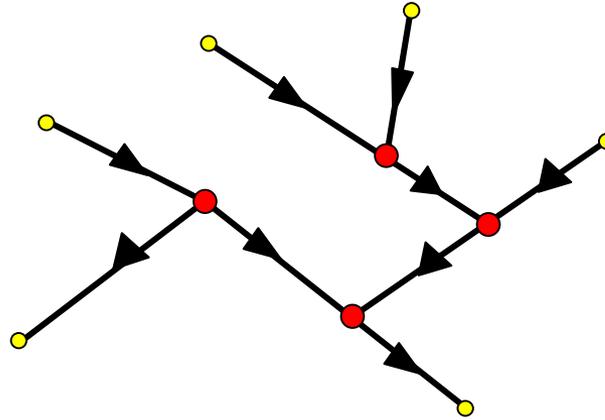- <u>Parabolic part</u>: Crank-Nicolson with finite differences in space

$$\phi_i^{n+1,j} = \phi_i^{n,j} - \frac{D_i k}{2h_i^2}\left(-\phi_i^{n,j+1} + 2\phi_i^{n,j} - \phi_i^{n,j-1}\right)$$

$$- \frac{D_i k}{2h_i^2}\left(-\phi_i^{n+1,j+1} + 2\phi_i^{n+1,j} - \phi_i^{n+1,j-1}\right)$$

$$+ \frac{a_i k}{2}\left(u_i^{n+1,j} + u_i^{n,j}\right) - \frac{b_i k}{2}\left(\phi_i^{n+1,j} + \phi_i^{n,j}\right).$$

Computational resolution of sparse banded matrix

Extension of GA to networks [Bretti, Natalini, Ribot, 2014]

- Network (oriented graph) of arcs and nodes:

Each arc is parametrized as an interval [0,Li]

On each arc i, we assign the hyperbolic-parabolic model:

$$
\begin{cases}
u_t^i + v_x^i = 0, \\[2mm]
v_t^i + \lambda_i^2 u_x^i = \chi \phi_x^i\, u^i - v^i, \\[2mm]
\phi_t^i - D_i\, \phi_{xx}^i = a_i u^i - b_i \phi^i,
\end{cases}
$$

+ transmission conditions (internal nodes) and boundary conditions (external nodes)

Transmission conditions for u (internal nodes)

Transmission conditions for u- (incoming) e u+ (outgoing) for flux continuity at node p:

$$\begin{cases} u_i^-(L_i, t) = \sum_{j \in I_p} \xi_{i,j} u_j^+(L_j, t) + \sum_{j \in O_p} \xi_{i,j} u_j^-(0, t), \text{ if } i \in I_p, \\ u_i^+(0, t) = \sum_{j \in I_p} \xi_{i,j} u_j^+(L_j, t) + \sum_{j \in O_p} \xi_{i,j} u_j^-(0, t), \text{ if } i \in O_p, \end{cases}$$

$\xi_{i,j} \in [0, 1]$ distribution coefficients at internal nodes

+ Flux conservation conditions:

+ Energy dissipation conditions of linearized hyperbolic system

$$\sum_{i \in I_p \cup O_p} \lambda_i \xi_{i,j} = \lambda_j, \, j \in I_p \cup O_p$$

$$\sum_{j \in I_p \cup O_p} \xi_{i,j} = 1 \text{ for all } i \in I_p \cup O_p$$

Transmission conditions for ϕ (internal nodes)

Kedem-Katchalsky (KK) permeability conditions at inner nodes:

$$D_i \partial_n \phi_i = \sum_{j \in I_p \cup O_p} \kappa_{i,j}(\phi_j - \phi_i), \ i \in I_p \cup O_p$$

(flux continuity at node p)

$\kappa_{i,j}$ non-negative coefficients

We have flux conservation at internal nodes:

$$\sum_{i \in I_p \cup O_p} D_i \partial_n \phi_i = 0$$

under the condition:

$$\kappa_{i,j} = \kappa_{j,i}, \quad i,j = 1, \ldots, N$$

Analytical results on network

- Natalini-Guarguaglini (SIMA, 2015): homogeneous boundary data, global existence for small data;

- Guarguaglini (NHM, 2017): homogeneous boundary data, asymptotic behavior (existence and uniqueness of stationary solutions);

- Guarguaglini, preprint 2018: asymptotic behavior for non-homogeneous boundary data

Null flux boundary conditions at outer nodes [NR12]

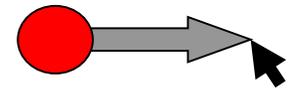Homogeneous Neumann condition for u:

$$u_i^+(.,t) = u_i^-(.,t) \iff v(.,t) = 0$$

and for ϕ:

$$\partial_x \phi_i(.,t) = 0$$

INCOMING ARCS:

OUTGOING ARCS:

Imposing mass conservation at each time step, the scheme for u is:

$$
\begin{cases}
u_{+,i}^{n+1,0} = u_{-,i}^{n+1,0} = \left(1 - \lambda_i \dfrac{k}{h_i}\right) u_{-,i}^{n,0} + k \left(\dfrac{\lambda_i}{h_i} - \dfrac{1}{4}\right) u_{-,i}^{n,1} \\
\qquad\qquad + \dfrac{k}{4} u_{+,i}^{n,1} - \dfrac{k}{4\lambda_i} f_i^{n,1}, \text{ if } i \in I_{out}, \\
u_{+,i}^{n+1,M+1} = u_{-,i}^{n+1,M+1} = \left(1 - \lambda_i \dfrac{k}{h_i}\right) u_{+,i}^{n,M+1} + k \left(\dfrac{\lambda_i}{h_i} + \dfrac{1}{4}\right) u_{+,i}^{n,M} \\
\qquad\qquad + \dfrac{k}{4} u_{-,i}^{n,M} + \dfrac{k}{4\lambda_i} f_i^{n,M_i}, \text{ if } i \in O_{out},
\end{cases}
$$

And we compute a numerical scheme for ϕ of order 2:

$$
\begin{cases}
\phi_i^{n+1,0} = \dfrac{4}{3}\phi_i^{n+1,1} - \dfrac{1}{3}\phi_i^{n+1,2}, & \text{if } i \in I_{\text{out}}, \\
\phi_i^{n+1,M_i+1} = \dfrac{4}{3}\phi_i^{n+1,M_i} - \dfrac{1}{3}\phi_i^{n+1,M_i-1}, & \text{if } i \in O_{\text{out}}.
\end{cases}
$$

Discrete transmission conditions for u (inner nodes) [Bretti, Natalini, Ribot, 2014]

Two conditions come from discretization of transmission conditions + two conditions come from mass conservation at each time step:

$$u_{+,i}^{n+1,M_i+1} = \delta_i \Big(u_{+,i}^{n,M_i+1} (1 - \frac{k}{2}) + u_{-,i}^{n,M_i+1} (1 - 2k\frac{\lambda_i}{h_i} + \frac{k}{2})$$
$$+ k u_{+,i}^{n,M_i} \big(2\frac{\lambda_i}{h_i} - \frac{1}{2}\big) - \frac{k}{2} u_{-,i}^{n,M_i} + \frac{k}{\lambda_i}(\frac{1}{2} f_i^{n,M_i+1} + \frac{1}{2} f_i^{n,M_i}) \Big), \text{ if } i \in I_p,$$

$$u_{-,i}^{n+1,0} = \delta_i \Big(u_{+,i}^{n,0}(1 - 2k\frac{\lambda_i}{h_i} + \frac{k}{2}) + u_{-,i}^{n,0}(1 - \frac{k}{2}) + \frac{k}{2} u_{+,i}^{n,1}$$
$$+ k u_{-,i}^{n,1} \big(2\frac{\lambda_i}{h_i} - \frac{1}{2}\big) - \frac{k}{\lambda_i}(\frac{1}{2} f_i^{n,1} + \frac{1}{2} f_i^{n,0}) \Big), \text{ if } i \in O_p.$$

$$\delta_i = h_i \Big(h_i + \sum_{j \in I_p \cup O_p} h_j \xi_{j,i} \Big)^{-1}$$

$$h_i = 2k\lambda_i,$$

CONSISTENCY CONDITION AT A NODE
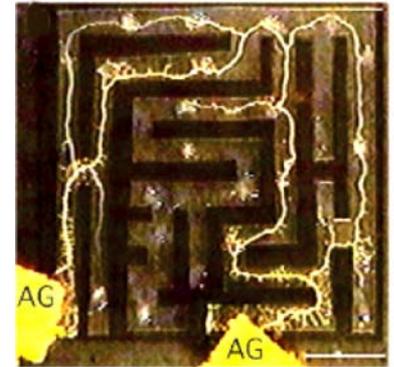
Discrete transmission conditions for φ (inner nodes)

KK discrete ai nodi conditions at inner nodes:

$$\phi_i^{n+1,M_i+1} = \frac{4}{3}\phi_i^{n+1,M_i} - \frac{1}{3}\phi_i^{n+1,M_i-1} + \frac{2}{3}\frac{h_i}{D_i}\sum_{j\in I_p}\kappa_{i,j}\left(\phi_j^{n+1,M_j+1} - \phi_i^{n+1,M_i+1}\right)$$

$$+ \frac{2}{3}\frac{h_i}{D_i}\sum_{j\in O_p}\kappa_{i,j}\left(\phi_j^{n+1,0} - \phi_i^{n+1,M_i+1}\right), \text{ if } i \in I_p,$$

$$\phi_i^{n+1,0} = \frac{4}{3}\phi_i^{n+1,1} - \frac{1}{3}\phi_i^{n+1,2} + \frac{2}{3}\frac{h_i}{D_i}\sum_{j\in I_p}\kappa_{i,j}\left(\phi_j^{n+1,M_j+1} - \phi_i^{n+1,0}\right)$$

$$+ \frac{2}{3}\frac{h_i}{D_i}\sum_{j\in O_p}\kappa_{i,j}\left(\phi_j^{n+1,0} - \phi_i^{n+1,0}\right), \text{ if } i \in O_p.$$

Non-homogeneous boundary conditions [Bretti-Natalini, 2018]

Modelling issue: need for more general boundary conditions to consider inflow/outflow at outer boundaries.
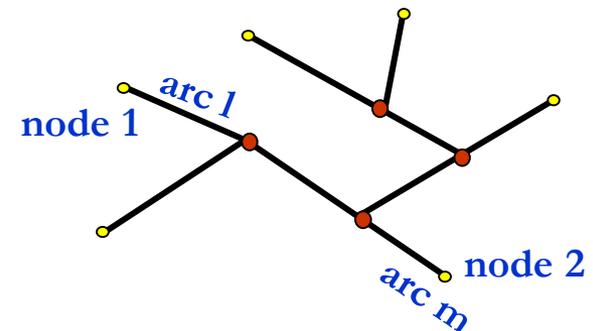

Inflow/outflow of cells:

$$\begin{cases} v_i(0,t) = w(0,t), & \text{if } i \in O_{out}, \\ v_i(L_i,t) = z(L_i,t), & \text{if } i \in I_{out}, \end{cases}$$

w,z: regular functions

Inflow/outflow of nutrients:

$$\partial_n \phi_i(.,t) + \beta \phi_i(.,t) = \bar{\phi}_i(t)$$

β≥0,
$\bar{\phi}$i : non-negative and eventually constant

node 1   arc 1

arc m   node 2

Note that in the case of inflow/outflow of cells total mass μ does **not** conserve and for the mass derivative at each time step we impose:

$$\mu'(t) = v_l(0,t) - v_m(L_m,t), \text{ for all } t > 0.$$

General outer boundary condition for u

Imposing a condition for the difference between total mass at two consecutive time steps and assuming, for instance, the inflow $w^{n+1,0} = \frac{2}{1+u_{+,l}^{n+1,0}+u_{-,l}^{n+1,0}}$ we get:

$$u_{+,l}^{n+1,0} := g_1^n(u_{-,l}^{n+1,0}) = \frac{1}{2\alpha_1}\left[-\beta_1^n - 2\alpha_1 u_{-,l}^{n+1,0} \right.$$
$$\left. + \sqrt{\left(\beta_1^n + 2\alpha_1 u_{-,l}^{n+1,0}\right)^2 - 4\alpha_1\left(\gamma_1^n + u_{-,l}^{n+1,0}\beta_1^n + \alpha_1(u_{-,l}^{n+1,0})^2\right)} \right],$$

Positivity of radicand to be checked at each time step

$$A^n = -\frac{2}{1+u_{+,l}^{n,0}+u_{-,l}^{n,0}} + h_l\left(-\frac{1}{k}(u_{+,l}^{n,0} + u_{-,l}^{n,0}) + (2\frac{\lambda_l}{h_l} - \frac{1}{2})u_{+,l}^{n,0} \right.$$
$$\left. + \frac{1}{2}u_{-,l}^{n,0} - \frac{1}{2}u_{+,l}^{n,1} - (2\frac{\lambda_l}{h_l} - \frac{1}{2})u_{-,l}^{n,1} + \frac{1}{\lambda_l}\left(\frac{1}{2}f_l^{n,1} + \frac{1}{2}f_l^{n,0}\right) \right),$$

$$\alpha_1 = \frac{h_l}{k},$$
$$\beta_1^n = \alpha_1 + A^n,$$
$$\gamma_1^n = A^n$$

General outer boundary condition for u

Imposing a condition for the difference between total mass at two consecutive time steps and assuming, for instance, the inflow $w^{n+1,0} = \frac{2}{1+u_{+,l}^{n+1,0}+u_{-,l}^{n+1,0}}$ we get:

$$u_{+,l}^{n+1,0} := g_1^n(u_{-,l}^{n+1,0}) = \frac{1}{2\alpha_1}\left[-\beta_1^n - 2\alpha_1 u_{-,l}^{n+1,0} \right.$$
$$\left. + \sqrt{\left(\beta_1^n + 2\alpha_1 u_{-,l}^{n+1,0}\right)^2 - 4\alpha_1\left(\gamma_1^n + u_{-,l}^{n+1,0}\beta_1^n + \alpha_1(u_{-,l}^{n+1,0})^2\right)} \right],$$

Positivity of radicand to be checked at each time step

$$u_{-,l}^{n+1,0} = u_{-,l}^{n,0}\left(1 - \frac{\lambda_l k}{h_l} - \frac{k}{4} - \frac{k}{4\lambda_l}\chi\phi_{x,l}^{n,0}\right) + g_1^{n-1}(u_{-,l}^{n,0})\left(\frac{k}{4} - \frac{k}{4\lambda_l}\chi\phi_{x,l}^{n,0}\right)$$
$$+ u_{-,l}^{n,1}\left(\frac{\lambda_l k}{h_l} - \frac{k}{4} - \frac{k\chi}{4\lambda_l}\frac{\phi_l^{n,2}-\phi_l^{n,0}}{2h_l}\right) + u_{+,l}^{n,1}\left(\frac{k}{4} - \frac{k\chi}{4\lambda_l}\frac{\phi_l^{n,2}-\phi_l^{n,0}}{2h_l}\right).$$

with: $\quad f_l^{n,0} = \chi u_l^{n,0}\phi_{x,l}^{n,0} \qquad f_l^{n,1} = \chi u_l^{n,1}\phi_{x,l}^{n,1} = \chi u_l^{n,1}\frac{\phi_l^{n,2}-\phi_l^{n,0}}{2h_l}$

MONOTONICITY CONDITION: k ≤ 1, provided that: $\quad -1 < \frac{\chi}{\lambda_l}\phi_{x,l}^{n,1} \leq 1$

General outer boundary condition for ф

$$\partial_n \phi_i(.,t) + \beta \phi_i(.,t) = \bar{\phi}_i(t),$$

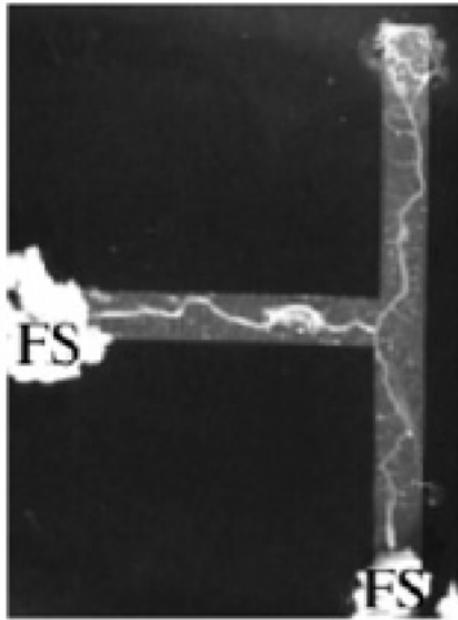Approximation of general boundary condition (independent on ф , i.e. β=0):

$$\begin{cases} \phi_i^{n+1,0} = \dfrac{4}{3}\phi_i^{n+1,1} - \dfrac{1}{3}\phi_i^{n+1,2} - \dfrac{2h_i}{3}\bar{\phi}_i^{n+1}, & \text{if } i \in O_{out}, \\[2ex] \phi_i^{n+1,M_i+1} = \dfrac{4}{3}\phi_i^{n+1,M_i} - \dfrac{1}{3}\phi_i^{n+1,M_i-1} + \dfrac{2h_i}{3}\bar{\phi}_i^{n+1}, & \text{if } i \in I_{out}. \end{cases}$$

Approximation of boundary condition dependent on ф (β=1 , $\overline{\phi}$=0) :

$$\begin{cases} \phi_i^{n+1,0}\left(1 + \dfrac{2h_i}{3}\right) = \dfrac{4}{3}\phi_i^{n+1,1} - \dfrac{1}{3}\phi_i^{n+1,2}, & \text{if } i \in I_{out}, \\[2ex] \phi_i^{n+1,M_i+1}\left(1 - \dfrac{2h_i}{3}\right) = \dfrac{4}{3}\phi_i^{n+1,M_i} - \dfrac{1}{3}\phi_i^{n+1,M_i-1}, & \text{if } i \in O_{out}. \end{cases}$$

T-shaped network

- Experiment to show d*ead-end cutting property [Tero, Kobayashi, Nakagaki, 2007]:*

(a) initial state   (b) final state

The arc with no-flux disappears

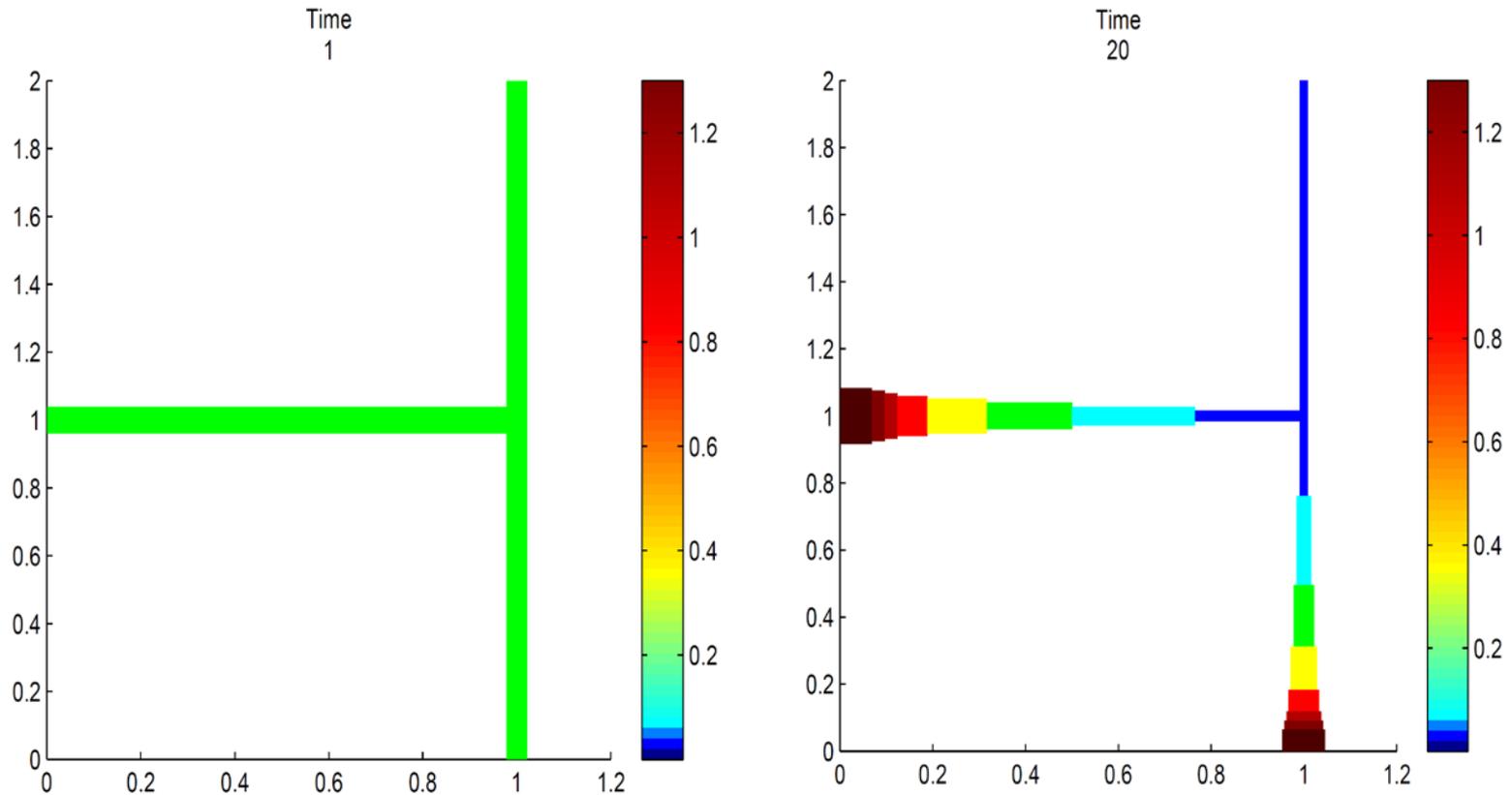# Numerical test : T-shaped network

Initial data on each arc:
- u(x,0) randomly equally distributed in [0.25, 0.35]
- ϕ (x,0) = 0

Boundary data:
- For ϕ :
$$\partial_x\phi_1(0,t) = -1, \quad \partial_x\phi_2(L_2,t) = 1$$

- Neumann homogeneous for u.

Distribution coefficients : ξ_{ij} =1/3 (equally distributed)

Numerical test: T-shaped network

The dead-end cutting property is obtained numerically with low density on the upper arc

Numerical test: diamond-like graph

$$L_1 = L_7 = 0.2, \ L_2 = L_4 = 0.3$$
$$L_3 = L_5 = 2, L_6 = 0.3$$

<u>Initial data on each arc:</u>

- u(x,0) randomly equally distributed in [0.45, 0.55]
- φ (x,0) = 0

<u>Inflow boundary conditions:</u>

- non homogeneous Neumann for u: $v_1(0,t) = \dfrac{2}{1 + u_1(0,t)}, \ v_7(L_7,t) = -\dfrac{2}{1 + u_7(L_7,t)}$

- non homogeneous Neumann for φ: $\partial_x \phi_1(0,t) = -1, \quad \partial_x \phi_7(L_7,t) = 1$

<u>Distribution coefficients</u>: $\xi_{ij} = 1/N_p$ (N_p: number of arcs connected at node p)

<u>Aim</u>: find asymptotically the shortest path connecting food sources node0-node5: path composed by arcs 1-2-6-4-7 (underlined by green line)
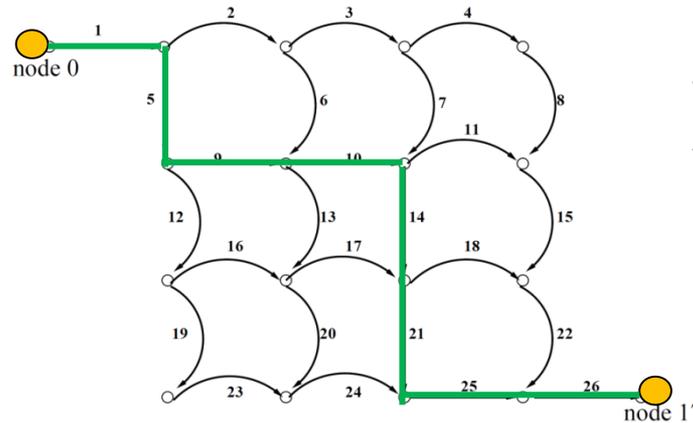
Diamond-like graph

node 2

node 0   node1   node4   node5

node3

$$L_1 = L_7 = 0.2, \ L_2 = L_4 = 0.3, \ L_3 = L_5 = 2, L_6 = 0.5$$

Time
130

The mass concentration is higher on the path of minimum length (time T= 130)

More complex network: 26 arcs – 18 nodes

As in [Borsche, Goettlich, Klar, Schillen, 2014], we consider:

$L_i = 0.5, \quad i = 1, 5, 9, 14, 21, 25, 26$

$L_i = 10$ elsewhere

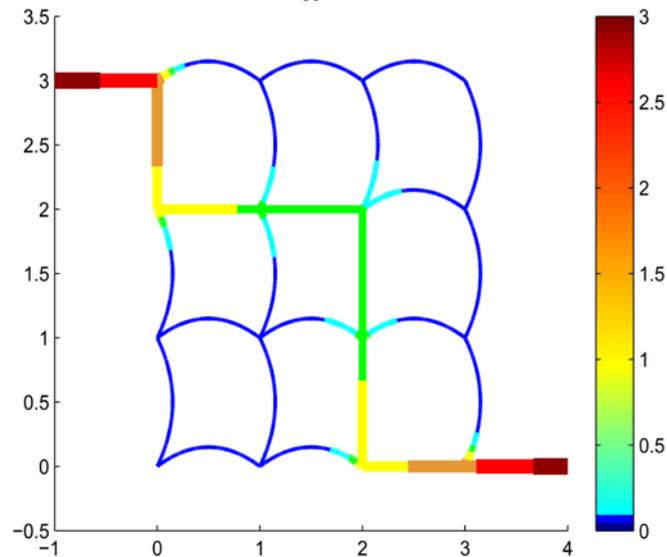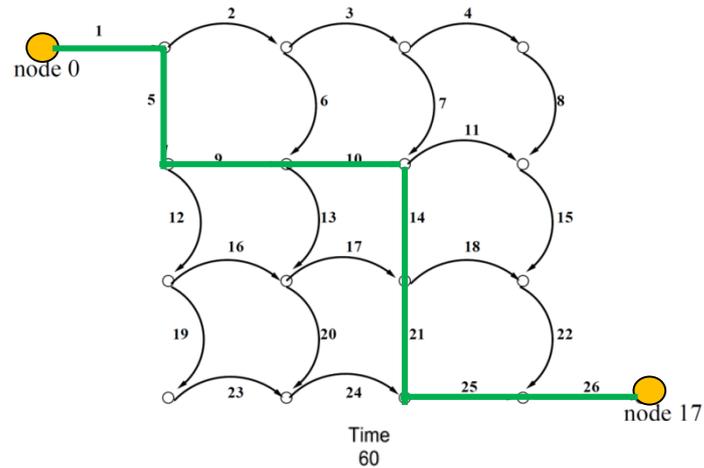and equally distributed transmission coefficients

Initial data:
- $u_i(x,0)$ randomly equally distribuited in [0, 0.1]
- $\phi_i(x,0) = 0$

Boundary conditions:
- non-homogeneous flux for u: $v_1(0,t) = \dfrac{2}{1 + u_1(0,t)}, \quad v_{26}(L_{26},t) = -\dfrac{2}{1 + u_{26}(L_{26},t)}$

- non homogeneous Neumann conditions for ϕ: $\partial_x \phi_1(0,t) = -1, \quad \partial_x \phi_{26}(0.5,t) = 1$
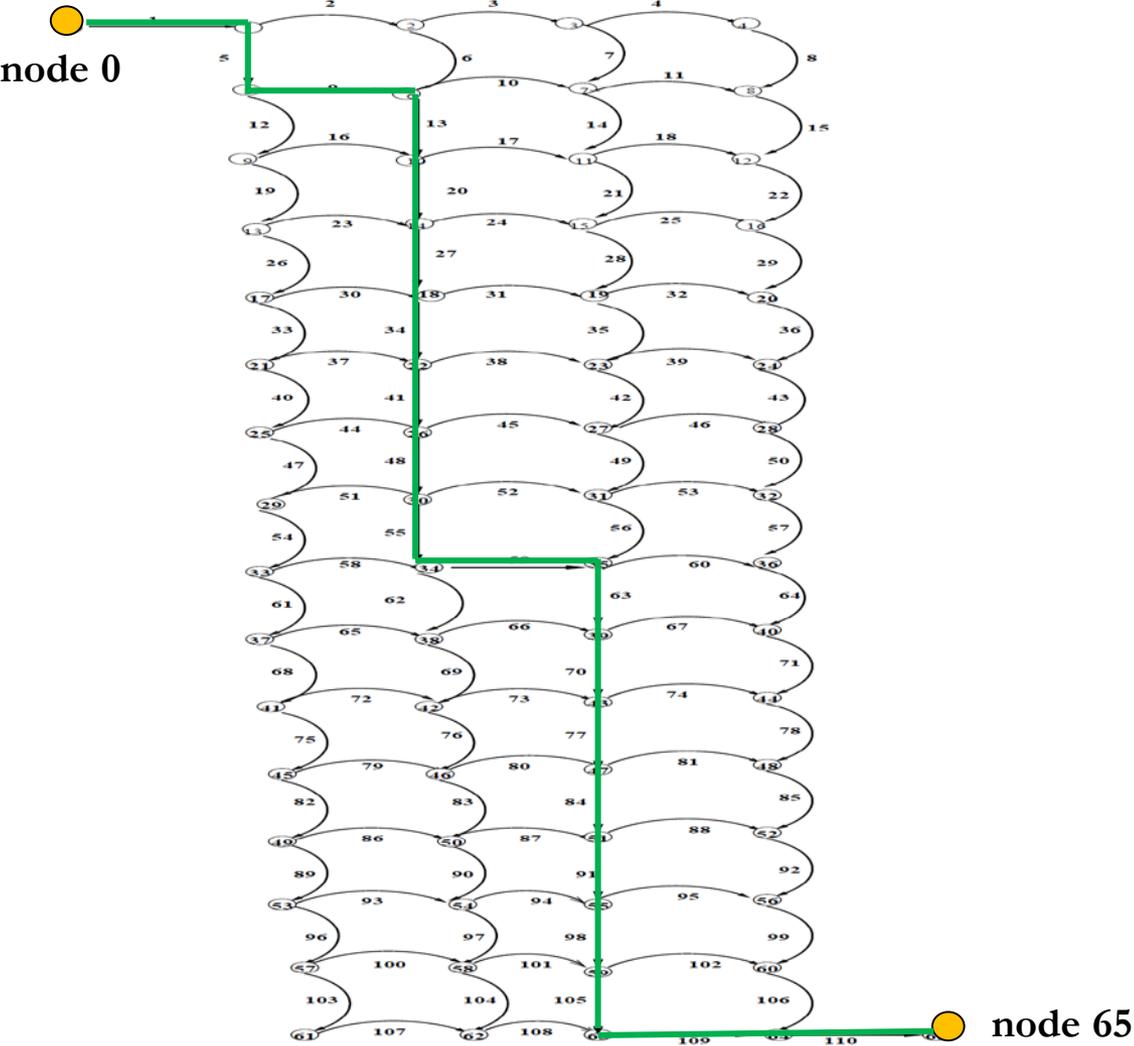
Aim: find the shortest path connecting food sources in node 0 and node 17: arcs 1-5-9-10-14-21-25-26 (underlined by green line)
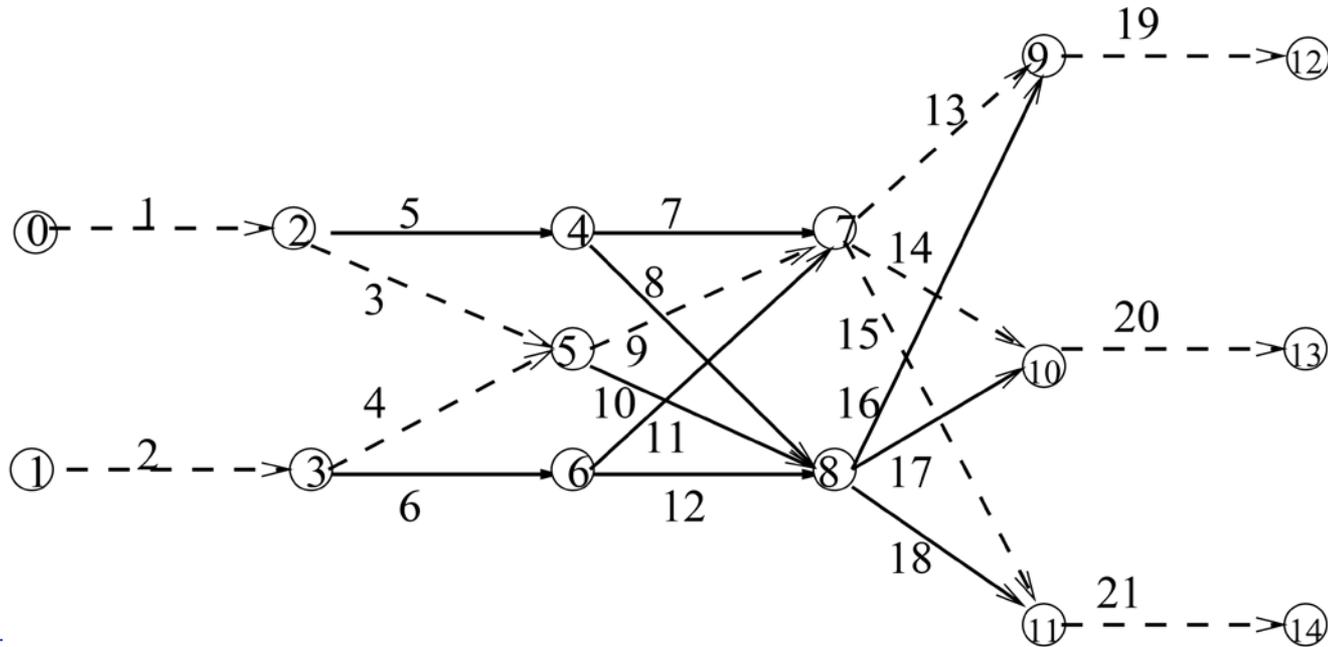
Network of 26 arcs – 18 nodes

The mass concentration is higher on the path of minimum length (time T= 60)

Test on a big network: 110 arcs – 66 nodes

We get asymptotically (T=200) the shortest path depicted with green line
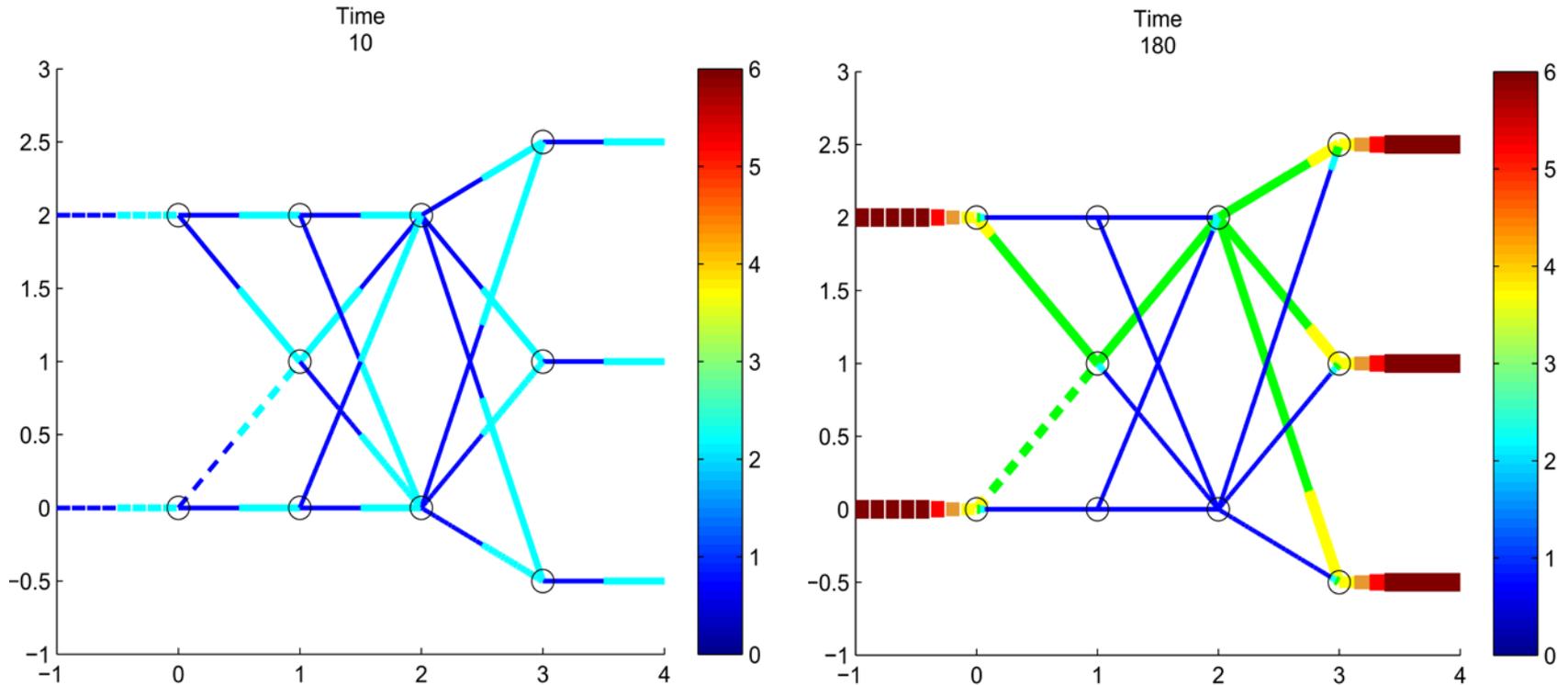
What happens with multiple food sources?

$$L_i = \begin{cases} 0.5 \text{ for arcs with dashed line} \\ 10 \text{ for arcs with continuous line} \end{cases}$$

$$\partial_x \phi_1(0,t) = -1 = \partial_x \phi_2(0,t), \quad \partial_x \phi_{19}(L_{19},t) = 1 = \partial_x \phi_{20}(L_{20},t) = \partial_x \phi_{21}(L_{21},t)$$

Aim: find the shortest path connecting food sources in node 0, node 1, node 12, node 13 and node 14: arcs 1-2-3-4-8-13-14-15-19-20-21 (depicted in dashed line)

Simulation with multiple food sources

The shortest path is obtained asymptotically even in this case

Latest reference paper

- G. Bretti - R. Natalini:

Numerical approximation of nonhomogeneous boundary conditions on networks for a hyperbolic system of chemotaxis modeling the Physarum dynamics; JCMSE vol. **18** (2018), pp. 85-115.

Thanks for your attention!