Multi-Agent Systems

Biology, Traffic flows, Social dynamics

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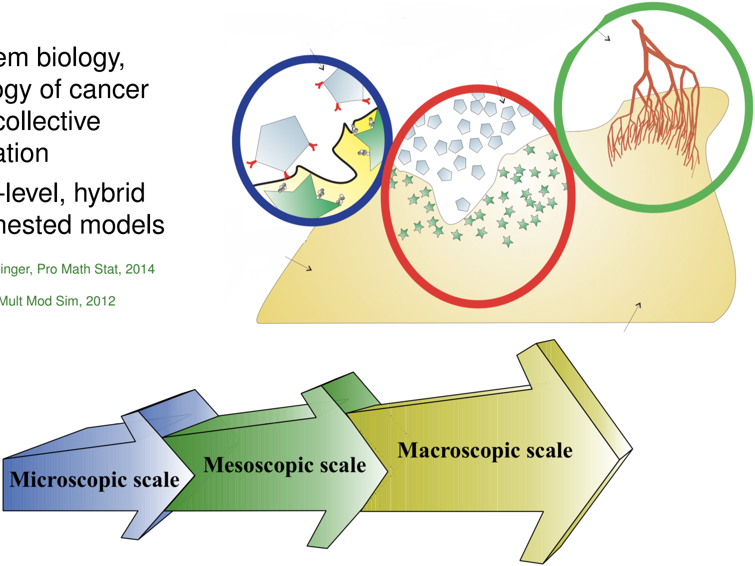
Kick-off meeting T2 - Politecnico di Torino, March, 14th, 2018

Multiscale modelling

- System biology, ecology of cancer and collective migration
- Multi-level, hybrid and nested models

Delitala, Hillen, Springer, Pro Math Stat, 2014

Scianna, Preziosi, Mult Mod Sim, 2012



Mathematical structures

- Boltzmann-type kinetic equations

$$\partial_t f + v\partial_x f = Q(f,\ f) + \Gamma(f)f$$
$$Q(f,\ f) = \iint \left(\frac{1}{|J|} f('v)f('w) - f(v)f(w) \right) dw$$

- Fokker-Planck equations

$$\partial_t f + \partial_v (K(f)f) = \partial_v^2 (D^2(v)f)$$
$$K(f) = \int k(v,\ w)f(w)\,dw$$

- Transport of measures

$$\mu_t = \gamma_t \# \mu_0$$

- Reaction-diffusion equations

$$\partial_t u = \nabla \cdot (\mathbf{D}\nabla u) + R(u)$$

- Nested cellular Potts models

$$H = \sum_{celli} \left(a_i - A_{targ}\right)^2 + H_{surf} + \ldots$$

- Conservation/balance laws

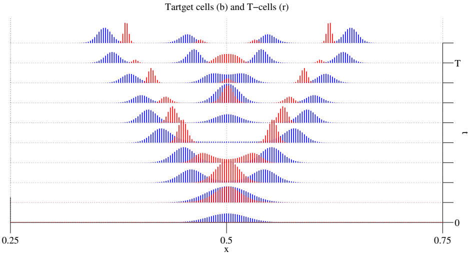
$$\partial_t \rho + \nabla \cdot (\rho \mathbf{v}) = \Gamma(\rho)$$

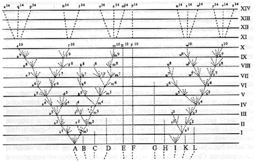
- Population dynamics

$$\begin{cases} \dot{x} = f(x, y) \\ \dot{y} = g(x, y) \end{cases}$$

Evolutionary dynamics

- Mutation and *selection principle in biology*
- Immune system *learning* and *immunoediting*





C. Darwin, 1859

- Asymptotic limits
- *Structured population with continuous variable*

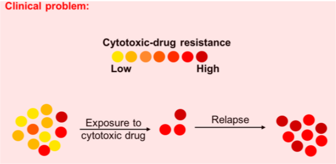
$$\frac{\partial}{\partial t} f_i(t,u) = \underbrace{\sum_{k=1}^{2} \int_U \mathcal{A}_k^i(u_*, u; \epsilon) f_k(t,u_*)\, du_* - f_i(t,u)}_{\text{EMT, mutations and renewal}} + \underbrace{\kappa(u) n_3(t) f_i(t,u)}_{\text{cell proliferation}}$$

$$\underbrace{-\mu_i(u) f_i(t,u)(\mathrm{n}_1(t) + \mathrm{n}_2(t))}_{\text{cell-cell competition}} - \underbrace{\mu^T g_1(t) f_i(t,u)}_{\text{destruction due to CAs}}$$

$$\underbrace{-\mu^T f_i(t,u) \int_V e^{-\theta^T (v^* - u)^2} g_2(t, v^*)\, dv^*}_{\text{destruction due to TTAs}},$$

Delitala, Lorenzi, J Theor Biol, 2012
Delitala, Lorenzi, J Math Anal Appl, 2012

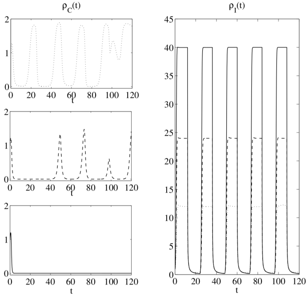
Evolutionary dynamics and therapies



- Therapeutic role of external agents: *selection for resistance*.
- Optimization of *immunotherapies*
- IBM and *micro-meso limit*

$$\frac{\partial}{\partial t} f_C(t,u) = \underbrace{\left(\kappa_C - \mu_C \varrho_C(t)\right) f_C(t,u)}_{\text{cancer growth and cell competition}} \underbrace{- f_C(t,u) \int_V \eta_{\theta_I}(|u-v|) f_I(t,v)\, dv}_{\text{immune competition}}$$

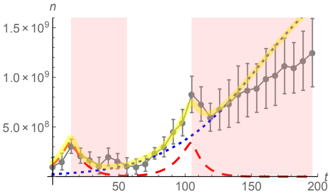
$$\frac{\partial}{\partial t} f_I(t,v) = \underbrace{\left[\int_U \eta_{\theta_E}(|u-v|) f_C(t,u)\, du + \kappa_P c_P(t)\right] f_I(t,v)}_{\text{clonal expansion and boosting of T-cell proliferation}} \underbrace{- \frac{\mu_I}{1+\mu_M c_M(t)} \varrho_I(t) f_I(t,v)}_{\text{homeostatic regulation and boosting of immune memory}}$$

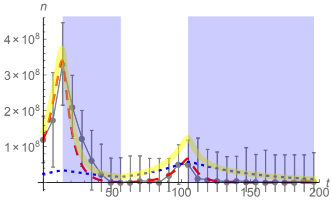


Delitala, Dianzani, Lorenzi, Melensi, Comput Math Appl, 2013
Lorenzi, Chisholm, Melensi, Lorz, Delitala, Immunology, 2015

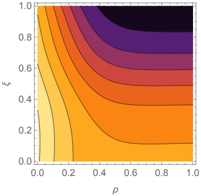
Evolutionary dynamics and drug resistance

- *Combination therapies*: dose and time protocols
- *Population dynamics* approach





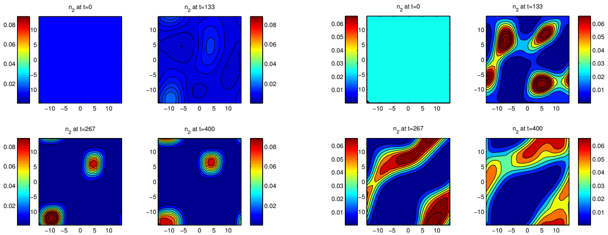
$$
\begin{aligned}
\frac{dx_1}{dt} &= \underbrace{r_1 x_1 - \frac{r_1}{K_1} x_1^2}_{\textit{proliferation}} - \underbrace{\frac{b_{12}}{K_1} x_1 x_2}_{\textit{competition}} - \underbrace{\frac{c_1}{K_1} x_1 z}_{\textit{predation}} - g_1(t) x_1 - \frac{h(t)}{K_1} x_1 z, \\
\frac{dx_2}{dt} &= r_2 x_2 - \frac{r_2}{K_2} x_2^2 - \frac{b_{21}}{K_2} x_1 x_2 - \frac{c_2}{K_2} x_2 z - g_2(t) x_2 - \frac{h(t)}{K_2} x_2 z, \\
\frac{dz}{dt} &= \underbrace{\beta z \left(1 - \frac{z}{H}\right)}_{\textit{proliferation}} + \underbrace{\frac{\alpha_1}{H} x_1 z + \frac{\alpha_2}{H} x_2 z}_{\textit{recognition}}.
\end{aligned}
$$



Piretto, Delitala, Ferraro, J Theor Biol, 2018

Tumor microenvironment

- Pattern formation, adhesion and diffusion in *co-culture of epithelial and mesenchymal cells*

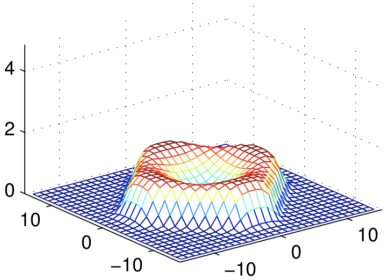


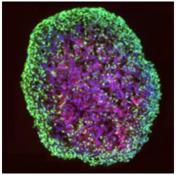
$$
\begin{aligned}
\partial_t f_1 + \mathbf{v} \cdot \nabla_{\mathbf{x}} f_1 \quad = \quad & \underbrace{\frac{1}{|V|}\left(1 + \frac{\mathbf{v} \cdot \nabla_{\mathbf{x}} n_4}{\beta + |\mathbf{v}||\nabla_{\mathbf{x}} n_4|}\right) n_1 - f_1}_{\text{random motion and chemotactic reorientation}} \\
+ \quad & \underbrace{\frac{(1-\gamma)}{|V|} n_1 \left(n_1 + n_3\right) - (n_1 + n_3) f_1}_{\text{homotypic adhesion}} \\
+ \quad & \underbrace{(\kappa - \mu\, N)\, f_1,}_{\text{proliferation and competition}}
\end{aligned}
$$

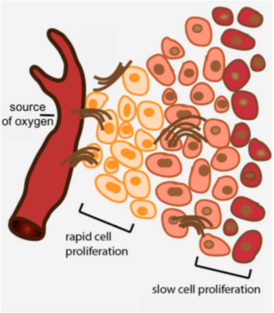
Delitala, Lorenzi, Math Biosci Eng, 2017
Delitala, Lorenzi, Appl Math Lett, 2013

Evolutionary dynamics and therapies

- Tumor micro-environment, hypoxic regions, and *evolutionary niche*.







$$\partial_t n_{20}(t,x) + \nabla_x \cdot (D \nabla_x n_{20}(t,x) - \Gamma[n_{40}] n_{20}(t,x)) = 0$$

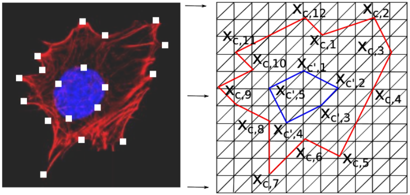
Fiandaca, Delitala, Lorenzi, in preparation

Nested Cellular Potts Model

- Interface between different modeling techniques
- Individual/discrete description of cell-level elements:
  - compartmentalized lattice- or vertex-based representation
  - stochastic energy-based laws for cell movement (Metropolis algorithm for Monte Carlo-Boltzmann thermodynamics)
- Continuous representation of molecular elements (RD Eqs.)

Scianna, Preziosi, Comp Biol Med, 2016

Scianna, Preziosi, Mult Mod Sim, 2012



$$H(t) = \lambda_a \sum_i (a_i - a_{targ})^2 + H_{force}(t) + \ldots$$

$$P_{\text{cell movement}}(t) = \min\left\{ e^{-\Delta H/T}, 1 \right\}$$

$$\partial_t c = \nabla \cdot D_c \nabla c + F(c)$$

Nested Cellular Potts Model

- Present topics:
  - cell migration in ECMs and microchannels

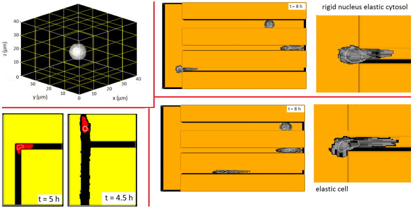
    Scianna, Preziosi, Wolf, Math Biosci Eng, 2013

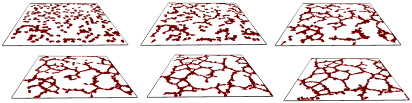
  - calcium signals and vascularization

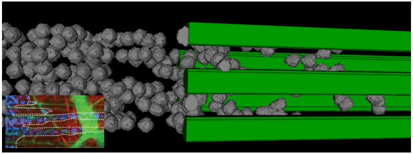
    Scianna, Munaron, Preziosi, Prog Biophys Mol Biol, 2011

  - reproduction of cell biophysical guidance mechanisms along muscle fibers

- Perspectives: Interface with continuous mechanics approaches for cell-substrate interactions







Hybrid Discrete-Continuous Models

- Individual/discrete cell description:
  - pointwise representation
  - ODEs for cell dynamics

$$m\frac{d^2\mathbf{x}_i}{dt^2}+\lambda_i\mathbf{v}_i+\sum_{j=1,j\neq i}^{N}\mu_{ij}\left(\mathbf{v}_i-\mathbf{v}_j\right)=\mathbf{F}_i$$

- Collective/continuous cell description:
  - use of cell densities
  - balance laws for cell dynamics

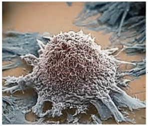
$$\partial_t\rho+\nabla\cdot(\rho\mathbf{v}_\rho)=\Gamma$$

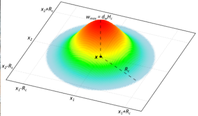
$$\mathbf{v}_i=\sum_{j=1}^{N}\mathbf{K}(\mathbf{x}_i,\mathbf{x}_j)+\int_\Omega\mathbf{H}(\xi,\mathbf{x}_i)\rho(\xi)\,d\xi$$

- Derivation of integro-differential equations with non-local terms

$$\mathbf{v}_\rho(\mathbf{y})=\sum_{i=1}^{N}\mathbf{K}(\mathbf{x}_i,\mathbf{y})+\int_\Omega\mathbf{H}(\xi,\mathbf{y})\rho(\xi)\,d\xi$$

- switches between cell representations via bubble-like functions or measure theory arguments





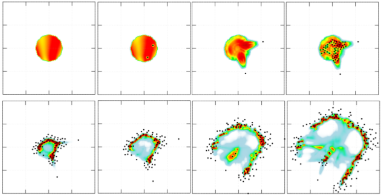
Hybrid Discrete-Continuous Models

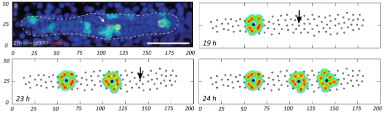
- Present topics:
  - inclusion of cell differentiation

    Colombi, Scianna, Tosin, J Math Biol, 2015
  - description of tumor growth and invasion
  - reproduction of zebrafish PLL formation

    Colombi, Scianna, Preziosi, J Math Biol, 2017
  - analysis of the H-stability of the system

    Carrillo, Colombi, Scianna, J Theor Biol, 2018





- Perspectives: Derivation of efficient numerical tools to deal with singular intercellular interaction kernels

Kinetic description of multi-agent systems

(Vehicular traffic, pedestrian crowds, opinion dynamics)

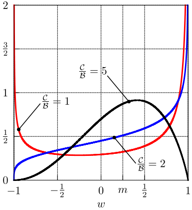
- Boltzmann-type integro-differential equations with or without space heterogeneity

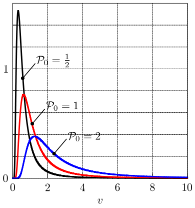
$$\partial_t f + v \cdot \nabla_x f = \int_V \int_\Omega \left(\frac{1}{|J|} f(x, {}'v) f(y, {}'w) - f(x, v) f(y, w) \right) dydw$$

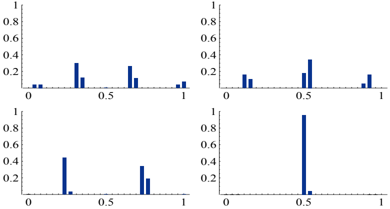
- Statistical description of emerging aggregate trends
  - Kinetic limits and Fokker-Planck equations

$$\partial_t f + \partial_v \left(f(v) \int_V K(v, w) f(w) dw \right) = \sigma^2 \partial_v^2 (D^2(v) f)$$

  - Asymptotic distributions, pattern formation, trends of statistical moments





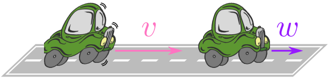


M. L. Bertotti, M. Delitala, *Z. Angew. Math. Phys.*, 2010, M. Delitala, T. Lorenzi, *Kinet. Relat. Models*, 2014, G. Visconti, M. Herty, G. Puppo, A. Tosin, *Multiscale Model. Simul.*, 2017, G. Toscani, A. Tosin, M. Zanella, *in preparation*

Microscopic binary interactions

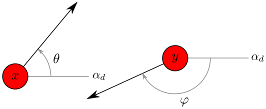
- Traffic: acceleration/deceleration

$$\begin{cases} v' = P(1-v) + (1-P)(Pw - v) + D(v)\eta \\ w' = w \end{cases}$$



- Crowds: collision avoidance

$$\begin{cases} \theta' = \theta + (1 - P(\theta,\varphi))(\alpha_d - \theta) + P(\theta,\varphi)\alpha_c \\ \varphi' = \varphi + (1 - P(\varphi,\theta))(\alpha_d - \varphi) + P(\varphi,\theta)\alpha_c \end{cases}$$



- Opinions: consensus/dissensus

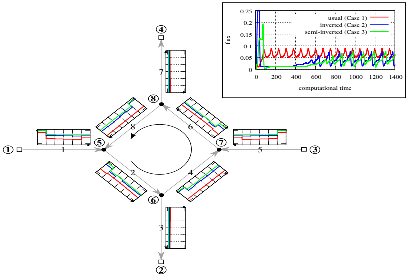
$$\begin{cases} v' = v + \gamma(w - v) + D(v)\eta \\ w' = w + \gamma(v - w) + D(w)\eta \end{cases}$$

- Binary control problems

$$v' = v + \Delta t(I(v,w) + u) + D(v)\eta, \quad u^* = \arg\min_{u\in\mathcal{U}} \int_t^{t+\Delta t} \left(\langle R(v,w)\rangle + \frac{\nu}{2}u^2\right)\, ds$$

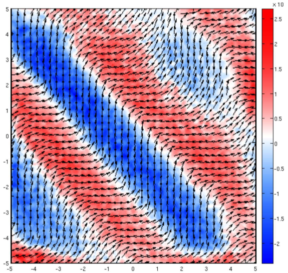
Macroscopic trends

- Traffic flow on road networks



L. Fermo, A. Tosin, *Math. Models Methods Appl. Sci.*, 2015

- Pedestrian counterflow



A. Festa, A. Tosin, M.-T. Wolfram, *Kinet. Relat. Models*, 2018

- Hydrodynamics from non-Maxwellian closures

$$\begin{cases} \partial_t \rho + \partial_x(\rho(u-m)) = 0 \\ \partial_t(\rho(u-m)) + \partial_x\left(\rho\left((u-m)^2 + \frac{\lambda}{2+\lambda}(1-u^2)\right)\right) = 0 \end{cases}$$

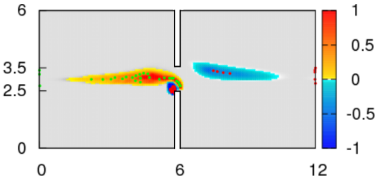
L. Pareschi, G. Toscani, A. Tosin, M. Zanella, *in preparation*

- Microscopically controlled equations at the macroscopic scale

A. Tosin, M. Zanella *in preparation*

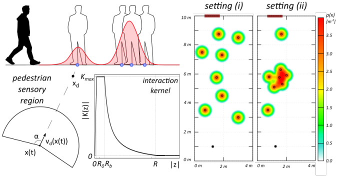
Hybrid discrete-continuous models

- Blended micro-macro description of 2D pedestrian flows



E. Cristiani, B. Piccoli, A. Tosin, *MS&A*, Springer, 2013

- Multiscale pedestrian perception in crowd dynamics



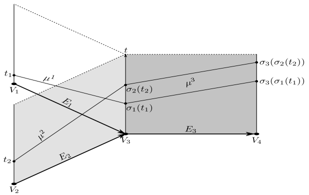
A. Colombi, M. Scianna, A. Tosin, *J. Coupled Syst. Multiscale Dyn.*, 2016

- Transport of measures

$$\mu_t = \gamma_t \# \mu_0, \qquad \begin{cases} \dot{\gamma}_t(x) = v(\gamma_t(x)) \\ v(x) = v_d(x) + \int_{S(t)} K(y-x)\, d\mu_t(y) \end{cases}$$

Hybrid discrete-continuous models

- Blended micro-macro description of traffic flow on road networks

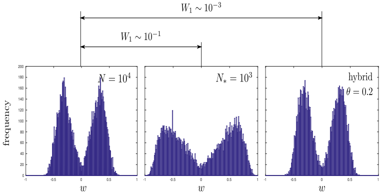


- Transport of measures on networks

$$\begin{cases} \partial_t \mu^j + \partial_x(\mu^j v_j[\mu^j]) = 0 \\ \mu^j_{t=0} = \mu^j_0 \\ \mu^j_{V_i} = \sum_{k=1}^{d_i^l} p^i_{kj}(t)\mu^k_{V_i} \end{cases}$$

F. Camilli, R. De Maio, A. Tosin, *J. Differential Equations*, 2018

- Multi-agent systems with symmetry breaking (opinion dynamics with polls)



- SDEs + Fokker-Planck equations

$$\begin{cases} dw_k &= [\theta K(w_k, \{w_h\}_{h=1}^N) \\ & \quad +(1-\theta)K[f](t, w_k)]dt \\ & \quad +\Theta dB_t^k \\ & \quad -(1-\Theta)D[f](t, w_k)dt \\ \partial_t f &= \partial_w((D[f]-K[f])f) \end{cases}$$

E. Cristiani, A. Tosin, *Multiscale Model. Simul.*, 2018