



Mathematical Theory and Applications of the Kinetic Theory of Active Particles

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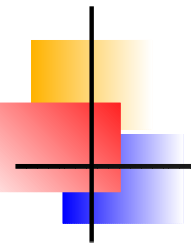
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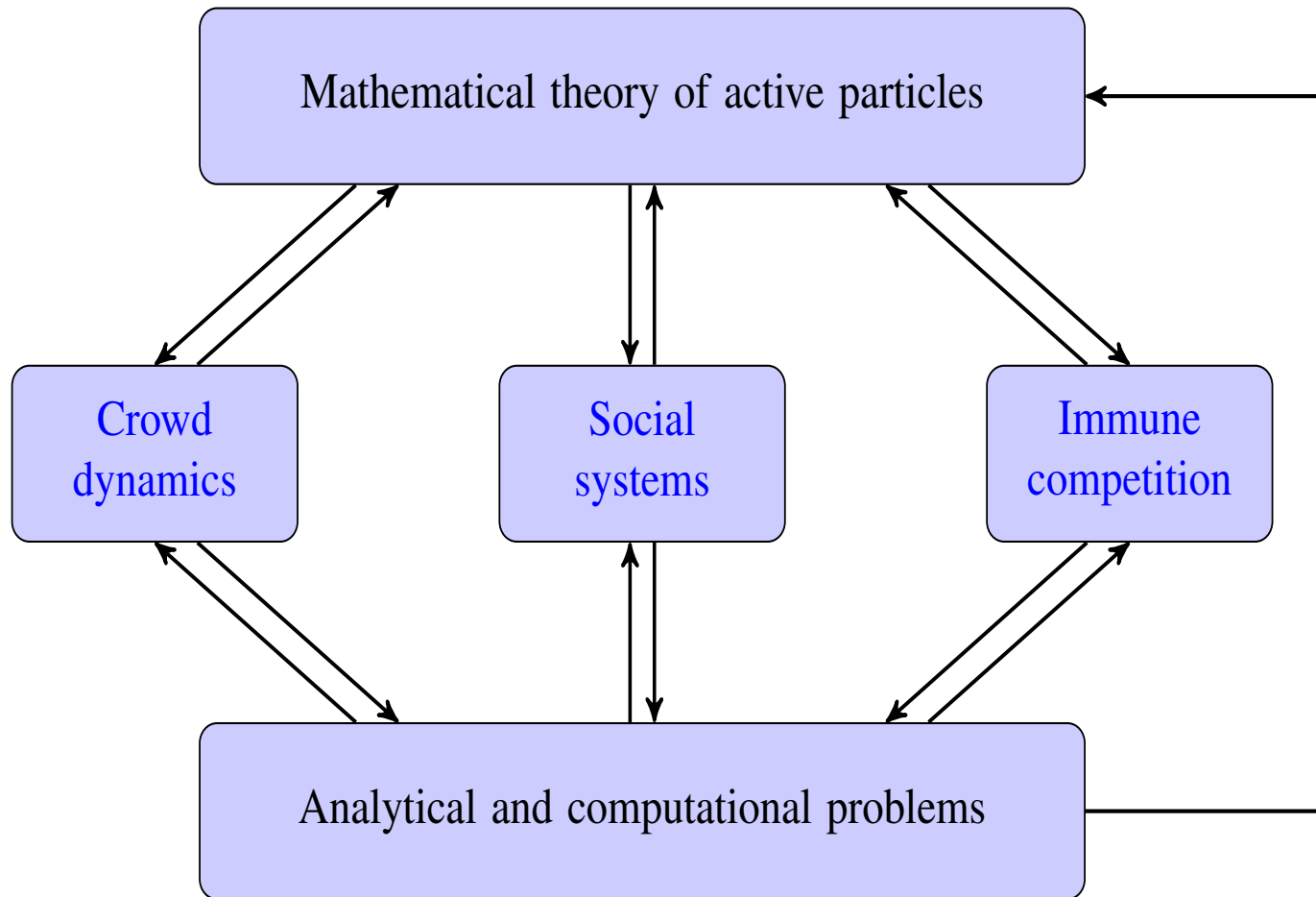
Porous Media Modelling in Biological Processes

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Theory and Application of the Kinetic Theory of Active Particles

Theory \rightarrow Applications \rightarrow Mathematical problems





Lecture 1 - Mathematical Theory

Quest toward a mathematical structure


$$\begin{aligned}\frac{\partial}{\partial \theta} M T(\xi) &= \frac{\partial}{\partial \theta} \int_{-\infty}^{\infty} f(x, \theta) dx = \int_{-\infty}^{\infty} \frac{\partial}{\partial \theta} f(x, \theta) dx \\ \frac{\partial}{\partial \theta} \ln f_{\text{max}}(\xi) &= \frac{(\xi - \theta)}{\sigma^2} f_{\text{max}}(\xi) - \frac{1}{2\sigma^2} \ln \left(\frac{1}{2\pi\sigma^2} \right) \\ \int_{-\infty}^{\infty} f(x) \cdot \frac{\partial}{\partial \theta} f(x, \theta) dx &= M \left(f(x) \frac{\partial}{\partial \theta} \ln f(x, \theta) \right) \int_{-\infty}^{\infty} f(x, \theta) dx \\ \int_{-\infty}^{\infty} f(x) \left(\frac{\partial}{\partial \theta} \ln f(x, \theta) \right) f(x, \theta) dx &= \int_{-\infty}^{\infty} f(x) \left(\frac{\partial}{\partial \theta} \ln f(x, \theta) \right) f(x, \theta) dx \\ \frac{\partial}{\partial \theta} M T(\xi) &= \frac{\partial}{\partial \theta} \int_{-\infty}^{\infty} f(x) f(x, \theta) dx = \int_{-\infty}^{\infty} \frac{\partial}{\partial \theta} f(x, \theta) f(x, \theta) dx\end{aligned}$$

- B.N., Knopoff D., and Soler J., On the difficult interplay between life, “complexity”, and mathematical sciences, *Math. Models Methods Appl. Sci.*, **23** (10) (2013), 1861–1913.



Lecture 1 - Mathematical Theory

Strategy

1. Understanding the links between the dynamics of living systems and their complexity features;
2. Understanding the multiscale features of living systems;
3. Derivation a general mathematical structure, consistent with the aforesaid features, with the aim of offering the conceptual framework toward the derivation of specific models;
4. Derivation of specific models corresponding to well defined classes of systems by implementing the structure by suitable micro-scale models of individual-based interactions;
5. Validation by quantitative comparison empirical data and assessment of their ability to depict qualitatively emerging behaviors.



Lecture 1 - Mathematical Theory

Five Common Features and Sources of Complexity

- 1. Ability to express a strategy:** Living entities are capable to develop specific *strategies* and *organization abilities* that depend on the state of the surrounding environment.
- 2. Heterogeneity:** The ability to express a strategy is not the same for all entities as *expression of heterogeneous behaviors* is a common feature of a great part of living systems.
- 3. Learning ability:** Living systems receive inputs from their environments and have the ability to learn from past experience.
- 4. Interactions:** Interactions are nonlinearly additive and involve immediate neighbors, but in some cases also distant entities.
- 5. Darwinian mutations and selection:** All living systems are evolutionary, as birth processes can generate entities more fitted to the environment, who in turn generate new entities again more fitted to the outer environment.



Lecture 1 - Mathematical Theory

Representation of a large system of interacting entities called active particles

- The description of the overall state of the system is delivered by the *one-particle distribution function*

$$f_i = f_i(t, \mathbf{x}, \mathbf{v}, u) = f_i(t, \mathbf{w}) : [0, T] \times \Omega \times D_{\mathbf{v}} \times D_u \rightarrow \mathbf{R}_+,$$

such that $f_i(t, \mathbf{x}, \mathbf{v}, u) d\mathbf{x} d\mathbf{v} du = f_i(t, \mathbf{w}) d\mathbf{w}$ denotes the number of active particles whose state, at time t , is in the interval $[\mathbf{w}, \mathbf{w} + d\mathbf{w}]$ of the i -th functional subsystem (still to be defined).

- $\mathbf{w} = \{\mathbf{x}, \mathbf{v}, u\}$ is an element of the *space of the microscopic states*.
- \mathbf{x} and \mathbf{v} represent the *mechanical variables*.
- u is the *activity variable* which models the strategy expressed in each functional subsystem.



Lecture 1 - Mathematical Theory

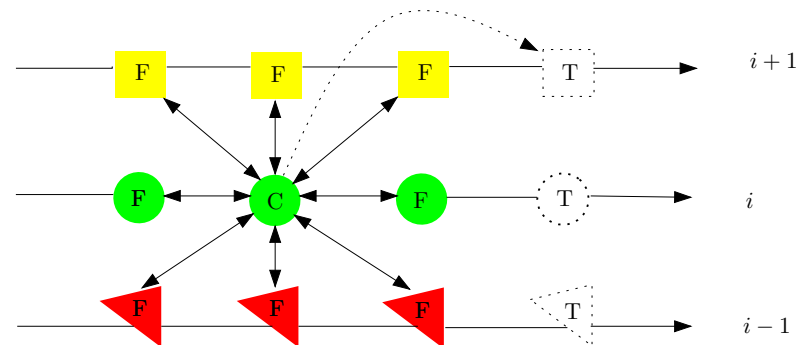
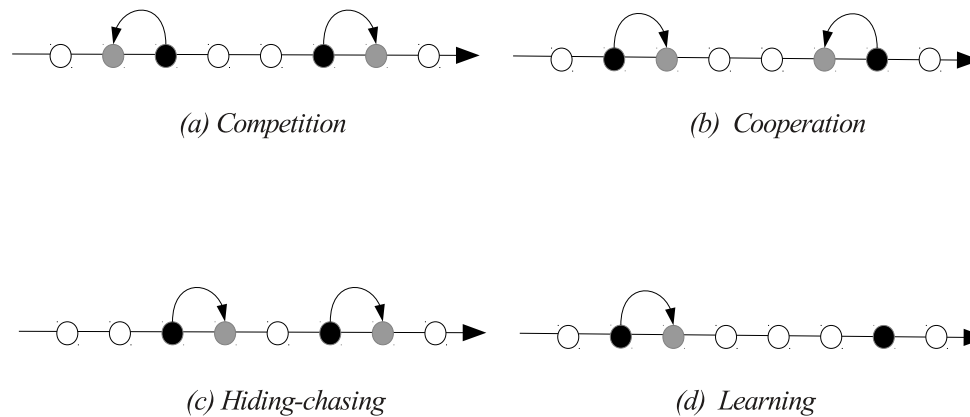
Stochastic Games

Interactions by evolutionary stochastic games: Living entities, at each interaction, *play a game* with an output that depends on their strategy often related to surviving and adaptation abilities. The output of the game generally is not deterministic even when a causality principle is identified.

1. **Competitive (dissent):** When one of the interacting particle increases its status by taking advantage of the other, obliging the latter to decrease it. Therefore the competition brings advantage to only one of the two.
2. **Cooperative (consensus):** When the interacting particles exchange their status, one by increasing it and the other one by decreasing it. Therefore, the interacting active particles show a trend to share their micro-state.
3. **Learning:** One of the two modifies, independently from the other, the micro-state, in the sense that it learns by reducing the distance between them.
4. **Hiding-chasing:** One of the two attempts to increase the overall distance from the other, which attempts to reduce it.

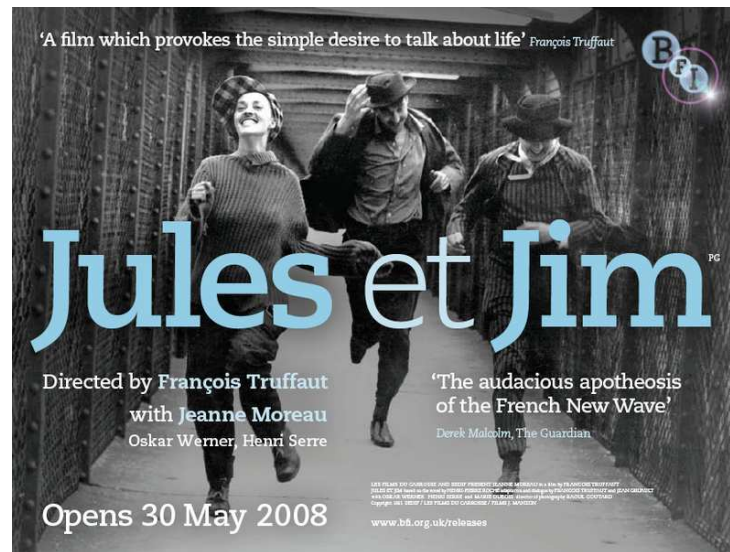
Lecture 1 - Mathematical Theory

Pictorial illustration, where black and grey bullets denote, respectively, the pre- and post-interaction states.



Lecture 1 - Mathematical Theory

Interactions among individuals need not have an additive linear character. As a consequence, the global impact of a given number of entities (field entities) over a single one (test entity) cannot be assumed to merely consist in the linear superposition of the actions exerted individually by single field entities. **This nonlinear feature represents a serious conceptual difficulty** to the derivation, and subsequent analysis, of mathematical models for that type of systems.





Lecture 1 - Mathematical Theory

- *J. Hofbauer and K. Sigmund*, Evolutionary game dynamics, *Bull. Am. Math. Society*, **40** 479-519, (2003).

Evolutionary game theory deals with entire population of players, all programmed to use the same strategy (or type of behaviour). Strategies with higher payoff will spread within the population, this can be achieved by learning, by copying or inheriting strategies, or even by infection. The payoffs depend on the actions of the coplayers and hence on the frequencies of the strategies within the population. Since these frequencies change according to the payoffs, this leads to a feedback loop. The dynamics of this feedback loop is the object of evolutionary game theory.

E. Mayr, **Populations, Species, and Evolution**, Harward University Press, (1970).

E. Mayr, **What Evolution Is**, Basic Books, New York, (2001).



Lecture 1 - Mathematical Theory

Interactions by evolutionary stochastic games:

- **Functional subsystems:** The overall system is subdivided into several populations, called **functional subsystems**, of entities called **active particles**, which express the same strategy.
- **Test** particles of the i -th functional subsystem with microscopic state, at time t , delivered by the variable $(\mathbf{x}, \mathbf{v}, u) := \mathbf{w}$, whose distribution function is $f_i = f_i(t, \mathbf{x}, \mathbf{v}, u) = f_i(t, \mathbf{w})$. The test particle is assumed to be representative of the whole system.
- **Field** particles of the k -th functional subsystem with microscopic state, at time t , defined by the variable $(\mathbf{x}^*, \mathbf{v}^*, u^*) := \mathbf{w}^*$, whose distribution function is $f_k = f_k(t, \mathbf{x}^*, \mathbf{v}^*, u^*) = f_k(t, \mathbf{w}^*)$.
- **Candidate** particles, of the h -th functional subsystem, with microscopic state, at time t , defined by the variable $(\mathbf{x}_*, \mathbf{v}_*, u_*) := \mathbf{w}_*$, whose distribution function is $f_h = f_h(t, \mathbf{x}_*, \mathbf{v}_*, u_*) = f_h(t, \mathbf{w}_*)$.



Lecture 1 - Mathematical Theory

Mathematical Structures: Models with Space Dynamics

H.1. Candidate or test particles in \mathbf{x} , interact with the field particles in the interaction domain $\mathbf{x}^* \in \Omega$. Interactions are weighted by the *interaction rate* $\eta_{hk}[\mathbf{f}]$ supposed to depend on the local distribution function in the position of the field particles.

H.2. A candidate particle modifies its state according to the probability density: $\mathcal{C}_{hk}^i[\mathbf{f}](\mathbf{v}_* \rightarrow \mathbf{v}, u_* \rightarrow u | \mathbf{w}_*, \mathbf{w})$, which denotes the probability density that a candidate particles of the h -subsystems with state $\mathbf{w}_* = \{\mathbf{x}_*, \mathbf{v}_*, u_*\}$ reaches the state $\{\mathbf{x} = \mathbf{x}_*, \mathbf{v}, u\}$ in the i -th subsystem after an interaction with the field particles of the k -subsystems with state $\mathbf{w}^* = \{\mathbf{x}^*, \mathbf{v}^*, u^*\}$.

H.3. A candidate particle, in \mathbf{x} , can proliferate, due to encounters with field particles in \mathbf{x}^* , with rate $\mu_{hk} \mathcal{P}_{hk}^i[\mathbf{f}]$, which denotes the proliferation rate into the functional subsystem i , due the encounter of particles belonging the functional subsystems h and k . Destructive events occur only within the same functional subsystem with rate $\mu_{ik} \mathcal{D}_{ik}[\mathbf{f}]$.



Lecture 1 - Mathematical Theory

Balance within the space of microscopic states and Structures

Variation rate of the number of active particles

$$\begin{aligned} &= \text{Inlet flux rate caused by conservative interactions} \\ &+ \text{Inlet flux rate caused by proliferative interactions} \\ &- \text{Outlet flux rate caused by destructive interactions} \\ &- \text{Outlet flux rate caused by conservative interactions,} \end{aligned}$$

where the inlet flux includes the dynamics of mutations.

This balance relation corresponds to the following structure:

$$(\partial_t + \mathbf{v} \cdot \partial_{\mathbf{x}}) f_i(t, \mathbf{x}, \mathbf{v}, u) = (J_i^C - J_i^L + J_i^P - J_i^D)[\mathbf{f}](t, \mathbf{x}, \mathbf{v}, u),$$

where the various terms J_i can be formally expressed, consistently with the definition of η , μ , \mathcal{C} , \mathcal{P} , and \mathcal{D} .

- *Michail Gromov*, In a Search for a Structure, Part 1: On Entropy, *Preprint*, (2013), <http://www.ihes.fr/~gromov/>.



Lecture 1 - Mathematical Theory

Mathematical Structures

$$J_i^C = \sum_{h,k=1}^n \int_{\Omega \times D_u^2 \times D_v^2} \eta_{hk}[\mathbf{f}](\mathbf{w}_*, \mathbf{w}^*) \mathcal{C}_{hk}^i[\mathbf{f}](\mathbf{v}_* \rightarrow \mathbf{v}, u_* \rightarrow u | \mathbf{w}_*, \mathbf{w}^*, u_*) \\ \times f_h(t, \mathbf{x}, \mathbf{v}_*, u_*) f_k(t, \mathbf{x}^*, \mathbf{v}^*, u^*) d\mathbf{x}^* d\mathbf{v}_* d\mathbf{v}^* du_* du^*,$$

$$J_i^L = \sum_{k=1}^n f_i(t, \mathbf{x}, \mathbf{v}) \int_{\Omega \times D_u \times D_v} \eta_{ik}[\mathbf{f}](\mathbf{w}_*, \mathbf{w}^*) f_k(t, \mathbf{x}^*, \mathbf{v}^*, u^*) d\mathbf{x}^* d\mathbf{v}^* du^*,$$

$$J_i^P = \sum_{h,k=1}^n \int_{\Omega \times D_u^2 \times D_v} \mu_{hk}[\mathbf{f}](\mathbf{w}_*, \mathbf{w}^*) \mathcal{P}_{hk}^i[\mathbf{f}](u_*, u^*) \\ \times f_h(t, \mathbf{x}, \mathbf{v}, u_*) f_k(t, \mathbf{x}^*, \mathbf{v}^*, u^*) d\mathbf{x}^* d\mathbf{v}^* du_* du^*,$$

$$J_i^D = \sum_{k=1}^n f_i(t, \mathbf{x}, \mathbf{v}) \int_{\Omega \times D_u \times D_v} \mu_{ik}[\mathbf{f}](\mathbf{w}_*, \mathbf{w}^*) \mathcal{D}_{ik}[\mathbf{f}](u_*, u^*) \\ \times f_k(t, \mathbf{x}^*, \mathbf{v}^*, u^*) d\mathbf{x}^* d\mathbf{v}^* du^*.$$

Lecture 2 - Crowd Dynamics

Modeling crowd dynamics



- B.N., Bellouquid A., and Knopoff D., From the micro-scale to collective crowd dynamics, *SIAM Multiscale Model. Simul.*, **11** (2013), 943–963.
- B.N. and Bellouquid A., On multiscale models of pedestrian crowds - From mesoscopic to macroscopic, *Comm. Math. Sci.*, **13** (2015), 1649–1664.
- B.N. and Gibelli L., Toward a Mathematical Theory of Behavioural-Social Dynamics for Pedestrian Crowds, *Math. Models Methods Appl. Sci.*, **25** (2015).



Lecture 2 - Crowd Dynamics

Why a crowd is a social, hence complex, system?

- **Ability to express a strategy:** Walkers are capable to develop specific strategies, which depend on their own state and on that of the entities in their surrounding environment.
- **Heterogeneity and hierarchy:** The ability to express a strategy is heterogeneously distributed and includes, in addition to different walking abilities, also different objectives.
- **Nonlinear interactions:** Interactions are nonlinearly additive and involve immediate neighbors, but also distant individuals.
- **Social communication and learning ability:** Walkers have the ability to learn from past experience. Therefore, their strategic ability evolves in time due to inputs received from outside induced by the tendency to adaptation.
- **Influence of environmental conditions:** The dynamics is remarkably affected by the quality of environment.



Lecture 2 - Crowd Dynamics

Mesoscale (kinetic type) representation

- The system can be subdivided into different groups, called **functional subsystems**, of persons, called **active particles**.
- The approach of the so-called **behavioral crowd dynamics** introduces an additional microscopic variable $u \in [0, 1]$, which models the heterogeneous ability to express a strategy specific for each functional subsystem.
- The overall state of the system is described by the **one-particle distribution function** $f_i = f_i(t, \mathbf{x}, \mathbf{v}, u)$ such that $f_i(t, \mathbf{x}, \mathbf{v}, u) d\mathbf{x} d\mathbf{v} du$ denotes the number of active particles whose state, at time t , is in the elementary volume of the **space of the microscopic states**. Local density and flux are computed as follows:

$$\rho_i(t, \mathbf{x}) = \int_{D_{\mathbf{v}} \times D_u} f_i(t, \mathbf{x}, \mathbf{v}, u) d\mathbf{v} du ,$$

$$\mathbf{q}_i(t, \mathbf{x}) = \int_{D_{\mathbf{v}} \times D_u} \mathbf{v} f_i(t, \mathbf{x}, \mathbf{v}, u) d\mathbf{v} du ,$$



Lecture 2 - Crowd Dynamics

Step 1: Modeling the decision process of adjustment of the velocity direction

Three types of stimuli contribute to modify the walking direction:

1. desire to reach a well defined target, $\boldsymbol{\nu}_i^{(\tau)}$;
2. attraction toward the mean stream, $\boldsymbol{\nu}^{(s)}$;
3. attempt to avoid overcrowded areas, $\boldsymbol{\nu}^{(v)}$.

The preferred direction is defined by

$$\boldsymbol{\nu}_i^{(p)} = \frac{(1 - \rho)\boldsymbol{\nu}_i^{(\tau)} + \rho((1 - \beta)\boldsymbol{\nu}^{(v)} + \beta\boldsymbol{\nu}^{(s)})}{\left\| (1 - \rho)\boldsymbol{\nu}_i^{(\tau)} + \rho((1 - \beta)\boldsymbol{\nu}^{(v)} + \beta\boldsymbol{\nu}^{(s)}) \right\|}$$

where the direction of vacuum and stream are given by

$$\boldsymbol{\nu}^{(v)} = -\frac{\nabla_{\mathbf{x}}\rho}{|\nabla\rho|}, \quad \boldsymbol{\nu}^{(s)} = \frac{V}{|V|}$$

where $\beta \in [0, 1]$ a parameter which models the sensitivity to the stream with respect to the search of vacuum.



Lecture 2 - Crowd Dynamics

Step 2: Adjustment of the speed to the new density conditions

Two cases can be distinguished:

- The walker's speed is greater or equal than the mean speed. The walker either maintains its speed, if for instance there is enough space to overtake the leading walker, or decelerate to a speed which is as much lower as the higher is the density. It is reasonable to assume that the probability to decelerate increases with the congestion of the space and with the badness of the environmental conditions.
- The walker's speed is lower than the mean speed. The walker either maintains its speed or accelerate to a speed which is as much higher as the lower is the density, the higher is the gap between the mean speed and the preferred speed and the goodness are the environmental conditions.

$$\begin{aligned} \mathcal{C}(v_* \rightarrow \tilde{v}) = & \left\{ p_+ \delta(\tilde{v} - V^{(+)}) + (1 - p_+) \delta(\tilde{v} - v_*) \right\} H(V - v_*) \\ & \left\{ p_- \delta(\tilde{v} - V^{(-)}) + (1 - p_-) \delta(\tilde{v} - v_*) \right\} H(v_* - V) \end{aligned}$$

where $p_+ = \alpha\beta(1 - \rho)$ and $p_- = (1 - \alpha)(1 - \beta)\rho$.



Lecture 2 - Crowd Dynamics

Step 3: Adjustment of the velocity in the presence of boundaries

Walkers whose distance from the wall, d , is within a specified cutoff, d_w , modify their velocity \mathbf{v} to a new velocity \mathbf{v}_r , by reducing the normal component linearly with the distance from the wall but keeping the speed constant, that is

$$\mathbf{v}^{(r)} = \frac{d}{d_w} (\mathbf{v} \cdot \mathbf{n}) \mathbf{n} + \text{sign}(\mathbf{v} \cdot \boldsymbol{\tau}) \left[v^2 - \frac{d^2}{d_w^2} (\mathbf{v} \cdot \mathbf{n})^2 \right]^{1/2} \boldsymbol{\tau}$$

where \mathbf{n} and \mathbf{t} are the normal and tangent to the solid wall.

Interaction domain: Interactions occur within an interaction domain related to the local velocity and visibility. The *perceived density* ρ_θ^a along the direction θ is:

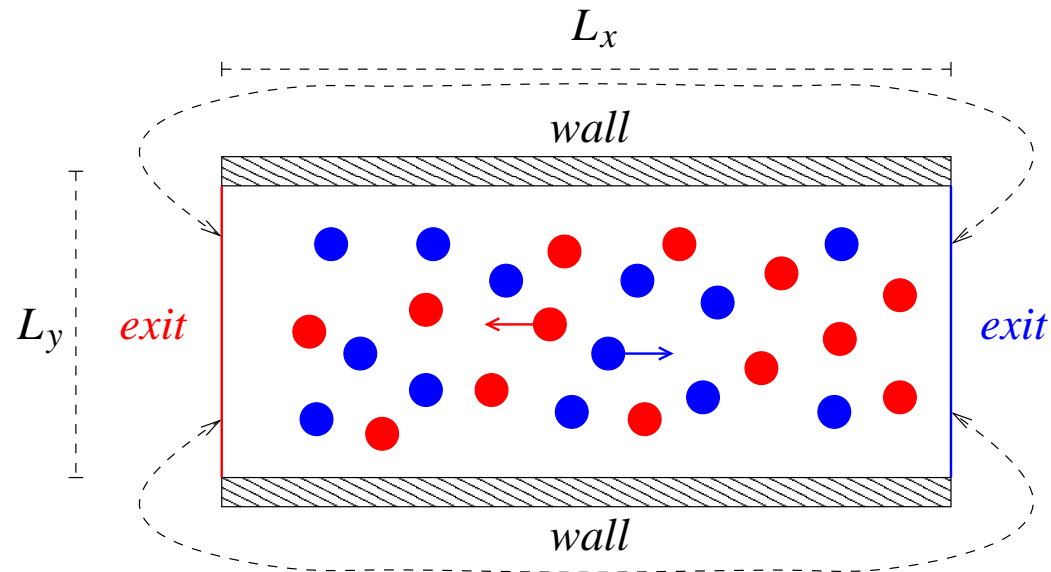
$$\rho_\theta^a = \rho_\theta^a[\rho] = \rho + \frac{\partial_\theta \rho}{\sqrt{1 + (\partial_\theta \rho)^2}} \left[(1 - \rho) H(\partial_\theta \rho) + \rho H(-\partial_\theta \rho) \right],$$

where ∂_θ denotes the derivative along the direction θ , while $H(\cdot)$ is the heaviside function $H(\cdot \geq 0) = 1$, and $H(\cdot < 0) = 0$.

$$\partial_\theta \rho \rightarrow \infty \Rightarrow \rho^a \rightarrow 1, \quad \partial_\theta \rho = 0 \Rightarrow \rho^a = \rho, \quad \partial_\theta \rho \rightarrow -\infty \Rightarrow \rho^a \rightarrow 0.$$

Lecture 2 - Crowd Dynamics

Individuals walking in a corridor with opposite directions

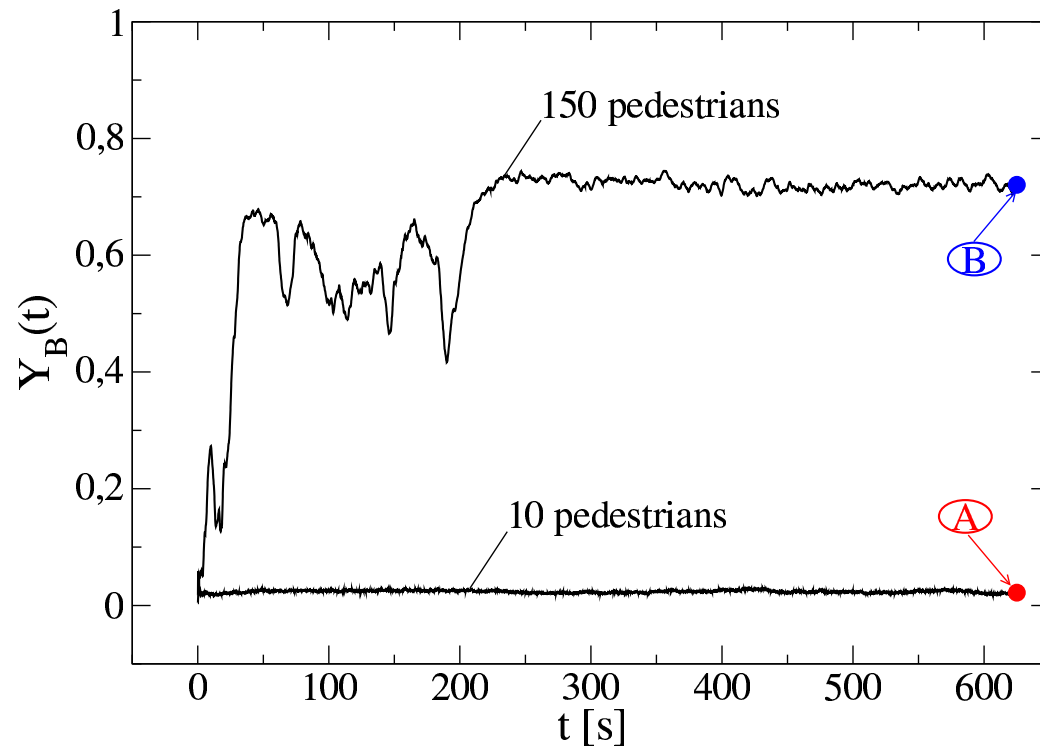


- The kinetic model of pedestrian crowds is applied to the problem of two groups of people walking in opposite directions.
- The segregation of walkers into lanes of uniform walking direction is quantitatively assessed by computing the band index

$$Y_B(t) = \frac{1}{L_x L_y} \int_0^{L_y} \int_0^{L_x} \frac{|\rho_1(t, \mathbf{x}) - \rho_2(t, \mathbf{x})|}{\rho_1(t, \mathbf{x}) + \rho_2(t, \mathbf{x})} dx dy$$

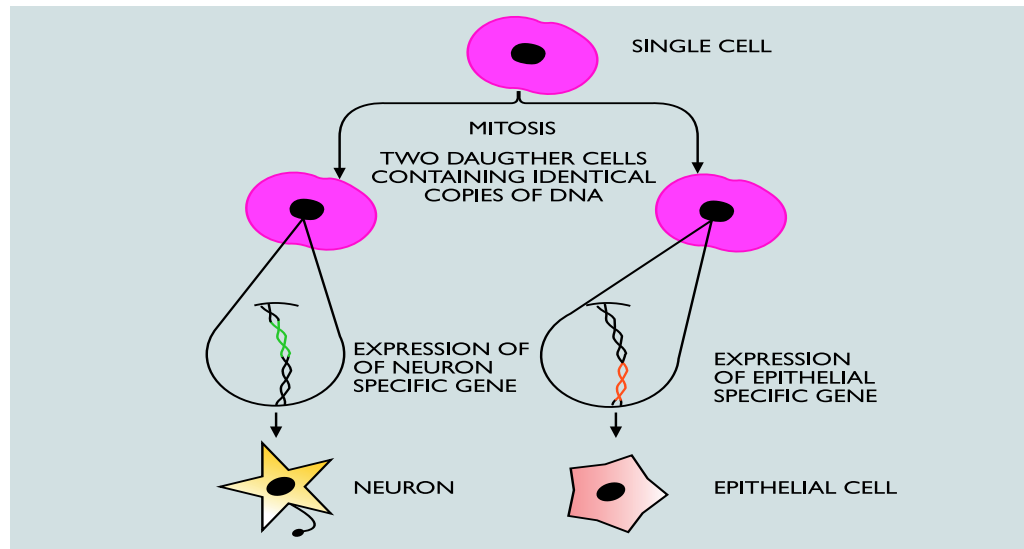
Lecture 2 - Crowd Dynamics

Pedestrians walking in a corridor with opposite directions



Lecture 3 - Darwinian Dynamics and Immune Competition

Modeling Darwinian Mutations and Selections and Immune Competition



Bellouquid A., De Angelis E., and Knopoff D., From the modeling of the immune hallmarks of cancer to a black swan in biology, *Math. Mod. Meth. Appl. Sci.*, 23, (2013), 949–978.

B.N. et al., On the Interplay between Mathematics and Biology - Hallmarks Looking for a New System Biology, *Physics of Life Review*, 12 (2015), 85-90.

R.A. Weinberg, *The Biology of Cancer*, Garland Sciences - Taylor and Francis, New York, (2007).



Lecture 3 - Darwinian Dynamics and Immune Competition

Immune competition

- **Malignant progression:** Mutations, self-sufficiency in growth signals, insensitivity to anti-growth signals, evading apoptosis, limitless replicative potential, evading immune system attack, and tissue invasion and metastasis, incorporate some aspects of genetic mutation, gene expression, and evolutionary selection.
- **Immune defence:** Immune cells *learn* the presence of carriers of a pathology and attempt to deplete them. It is a complex process, where cells from the *innate immunity* improve their action by learning the so-called *acquired immunity*.
- **Darwinian selection:** Can potentially initiate in each birth process, where mutations bring new genetic variants into populations and natural selection then screens them. In some cases, new cell phenotypes can originate from random mistakes during replication.

Lecture 3 - Darwinian Dynamics and Immune Competition

Decomposition into functional subsystems The model considers two types of active particles, namely epithelial and cancer cells, which move from the differentiate state to various levels of progression, and immune cells characterized by different values of activation.

↓	$i = 1$ Epithelial cells		$i = 5$ Innate immune cells	↓
↓	$i = 2$ First <i>hallmark</i>	←	$i = 6$ Acquired immunity 1	↓
↓	$i = 3$ Second <i>hallmark</i>	←	$i = 7$ Acquired immunity 2	↓
	$i = 4$ Third <i>hallmark</i>	←	$i = 8$ Acquired immunity 3	

Table Functional subsystems

- $i = 2$ corresponds to the ability to thrive in a chronically inflamed micro-environment;
- $i = 3$ to the ability to evade the immune recognition;
- $i = 4$ to the ability to suppress the immune reaction.



Lecture 3 - Darwinian Dynamics and Immune Competition

Mathematical structure

$$\begin{aligned}\frac{d}{dt} f_{ij}(t) &= J_{ij}[f](t) = C_{ij}[f](t) + P_{ij}[f](t) - D_{ij}[f](t) + L_{ij}[f](t) \\ &= \sum_{k=1}^n \sum_{p=1}^m \sum_{q=1}^m \eta_{ik}[f] \mathcal{B}_{ik}^{pq}(j)[f] f_{ip} f_{kq} - f_{ij} \sum_{k=1}^n \sum_{q=1}^m \eta_{ik}[f] f_{kq} \\ &= \sum_{h=1}^n \sum_{k=1}^n \sum_{p=1}^m \sum_{q=1}^m \eta_{hk}[f] \mu_{hk}^{pq}(ij) f_{hp} f_{kq} - f_{ij} \sum_{k=1}^n \sum_{q=1}^m \eta_{ik}[f] \nu_{ik}^{jq} f_{kq}, \\ &\quad + \lambda (f_{ij}^0 - f_{ij}),\end{aligned}$$

for $i = 1, \dots, 8$ and $j = 1, \dots, m$, and it is assumed that the activity variable attains values in the following discrete set: $I_u = \{0 = u_1, \dots, u_j, \dots, u_m = 1\}$. The overall state of the system is described by the distribution function

$$f_{ij} = f_{ij}(t), \quad i = 1, \dots, 8, \quad j = 1, \dots, m,$$

where the index i labels each subsystem, j labels the level of the activity variable, and $f_{ij}(t)$ represents the number of active particles from functional subsystem i that, at time t , have the state u_j .



Lecture 3 - Darwinian Dynamics and Immune Competition

Interactions

- **Conservative interactions:** Cells modify their activity within the same functional subsystem. A candidate h -particle with state u_p can experiment a conservative interaction with a field k -particle. The output of the interaction can be in the contiguous states u_{p-1} , u_p or u_{p+1} .
- **Net proliferative events:** Can generate, although with small probability, a daughter cell that presents genetic modifications with respect to the mother cell. A candidate h -particle (mother cell) can generate, by interacting with a field k -particle, a daughter cell, belonging either to the same functional subsystem with same state, or eventually to the following functional subsystem with the lowest activity value.
- **Destructive events:** The immune system has the ability to suppress a cancer cell. A h -candidate particle with state u_p , interacting with a field k -particle with state u_q can undergo a destructive action which occurs within the same state of the candidate particle.

Lecture 3 - Darwinian Dynamics and Immune Competition

Interactions

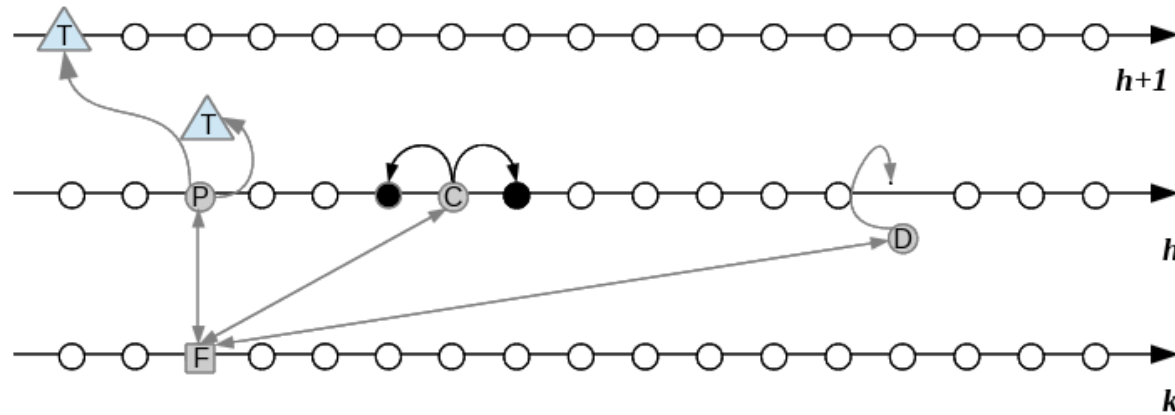


Figure 1: A h -candidate particle P (mother cell) by interaction with a k -field particle F proliferates giving a daughter cell T , belonging either to the same functional subsystem with same state (identical daughter), or to the following functional subsystem with the lowest activity value (mutated daughter). Candidate particle C can experiment a conservative interaction with the field particle F , with an output in the same functional subsystem. Finally, candidate particle D can be subject a destructive action which occurs within the same state.



Lecture 3 - Darwinian Dynamics and Immune Competition

Qualitative analysis and simulations

- The objective of the qualitative and computational analysis consists in understanding if the immune system, possibly thank also to therapeutical actions, has the ability to suppress cells of the last hallmark.
- Existence of solutions for arbitrary large times has been proved, while simulations have shown the whole panorama of the competition depending on a critical parameter that separate the situations where the immune system gains from those where it loses. It is the ratio between the mutation rates of the immune cells versus cancer cells, both corresponding to the last mutation.
- Simulations show different trajectories are obtained for the number density of tumor cells corresponding to increasing values of the ratio between the said parameter. The first trajectory shows that for low values of the parameter the model predicts a rapid growth of cancer cells due to the lack of contrast of the immune system. However, for increasing values of the parameter the trajectory shows a trend to an asymptotic value corresponding to a certain equilibrium. This asymptotic value decreases for increasing value of the parameter up to when the defence is strong enough to deplete the presence of tumor cells.

Lecture 3 - Darwinian Dynamics and Immune Competition

Simulations

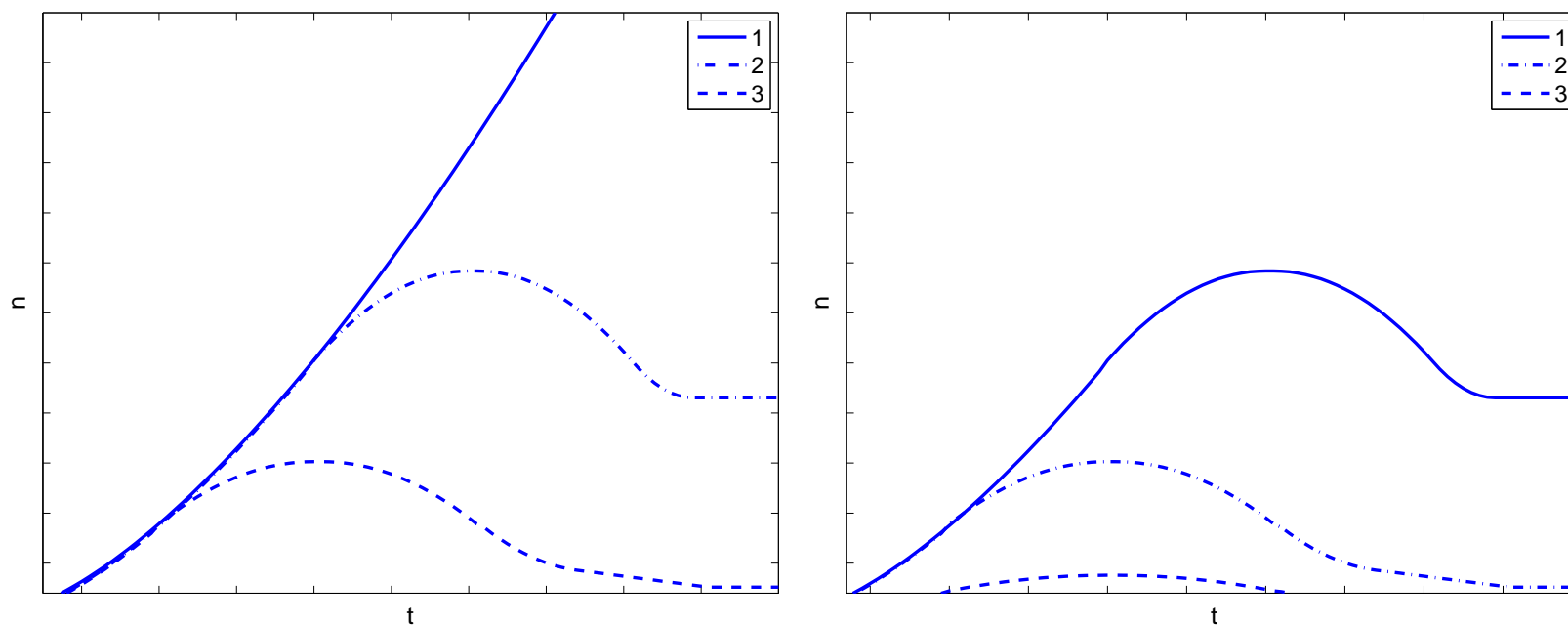


Figure 2: Mutations and evolution in competition with the immune system with the effect of therapeutical actions

Lecture 4 - New Trends in Behavioral Economy and Sociology



- B.N., Herrero M.A., Tosin A., On the Dynamics of Social Conflicts Looking for the Black Swan, *Kinet. Relat. Models*, 6(3), 459–479, (2013).
- Ajmone Marsan G., B. N., and Tosin A., **Complex Systems and Society – Modeling and Simulations**, *Springer Briefs*, Springer, New York, (2013).
- B.N., Colasuonno F., Knopoff D., and Soler J., From a Systems Theory of Sociology to Modeling the Onset and Evolution of Criminality, *Networks Heter. Media*, 10, 421-441, (2015).
- N.N. Taleb, **The Black Swan: The Impact of the Highly Improbable**, 2007.



Lecture 4 - New Trends in Behavioral Sociology

Preliminary Reasonings

- The dynamics of social and economic systems are necessarily based on individual behaviors, by which single subjects express, either consciously or unconsciously, a particular strategy, which is heterogeneously distributed. The latter is often based not only on their own individual purposes, but also on those they attribute to other agents.
- In the last few years, a radical philosophical change has been undertaken in social and economic disciplines. An interplay among Economics, Psychology, and Sociology has taken place, thanks to a new cognitive approach no longer grounded on the traditional assumption of rational socio-economic behavior. Starting from the concept of bounded rationality, the idea of Economics as a subject highly affected by individual (rational or irrational) behaviors, reactions, and interactions has begun to impose itself.
- A key experimental feature of such systems is that interaction among heterogeneous individuals often produces unexpected outcomes, which were absent at the individual level, and are commonly termed emergent behaviors. Mathematical sciences can significantly contribute to a deeper understanding of the relationships between individual behaviors and the collective social outcomes they spontaneously generate.



Lecture 4 - New Trends in Behavioral Sociology

Modeling strategy - Modeling on the Onset and Dynamics of Criminality

- The overall system is partitioned into functional subsystems, whose elements, called active particles, have the ability to collectively develop a common strategy;
- The strategy is heterogeneously distributed among the components and corresponds to an individual state, defined activity, of the active particles;
- The state of each functional subsystem is defined by a probability distribution over the activity variable;
- Active particles interact within the same functional subsystem as well as with particles of other subsystems, and with agents from the outer environment;
- Interactions generally are nonlinearly additive and are modeled as stochastic games, meaning that the outcome of a single interaction event can be known only in probability;
- The evolution of the probability distribution is obtained by a balance of particles within elementary volumes of the space of microscopic states, the inflow and outflow of particles being related to the aforementioned interactions.



Lecture 4 - New Trends in Behavioral Sociology

Functional subsystems, representation, and structure

$i = 1$ Normal citizens, whose microscopic state is identified by their wealth, which constitutes the attraction for the eventual perpetration of criminal acts.

$i = 2$ Criminals, whose microscopic state is given by their criminal ability, namely their ability to succeed in the perpetration of illegal acts.

$i = 3$ Detectives who chase criminals according to their individual ability.

Functional subsystem	Micro-state
$i = 1$, citizens	$u \in D_1$, wealth
$i = 2$, criminals	$u \in D_2$, criminal ability
$i = 3$, detectives	$u \in D_3$, experience/prestige

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$$\begin{aligned}
 \partial_t f_i(t, u) &= J_i[\mathbf{f}](t, u) = \\
 &= \sum_{h,k=1}^3 \int_{D_h} \int_{D_k} \eta_{hk}(u_*, u^*) \mathcal{B}_{hk}^i(u_* \rightarrow u | u_*, u^*) f_h(t, u_*) f_k(t, u^*) du_* du^* \\
 &\quad - f_i(t, u) \sum_{k=1}^3 \int_{D_k} \eta_{ik}(u, u^*) f_k(t, u^*) du^* \\
 &\quad + \int_{D_i} \mu_i(u_*, \mathbb{E}_i) \mathcal{M}_i(u_* \rightarrow u | u_*, \mathbb{E}_i) f_i(t, u_*) du_* \\
 &\quad - \mu_i(u, \mathbb{E}_i) f_i(t, u),
 \end{aligned}$$

where $f_i : [0, T] \times D_i \rightarrow \mathbf{R}_+$, $i = 1, 2, 3$. Moreover $\eta_{hk}(u_*, u^*)$ and $\mu_h(u_*, \mathbb{E}_h)$ are, respectively, the encounter rate of individual based interactions and that between a candidate h -particle and the mean activity. Moreover, $\mathcal{B}_{hk}^i(u_* \rightarrow u | u_*, u^*)$ and $\mathcal{M}_h(u_* \rightarrow u | u_*, \mathbb{E}_h)$ are, respectively, the probability density for the state transition of individual based interactions and that between a candidate h -particle and the mean activity.

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Interaction	Qualitative description	η
	Closer social states	
$\boxed{1} \leftrightarrow \textcircled{1}$	tend to interact more frequently	$\eta_{11}(u_*, u^*) = \eta^0 (1 - u_* - u^*)$
	Experienced lawbreakers	
$\boxed{2} \leftrightarrow \textcircled{2}$	are more expected to expose themselves	$\eta_{22}(u_*, u^*) = \eta^0 (u_* + u^*)$
	Experienced detectives	
$\boxed{2} \leftrightarrow \textcircled{3}$	are more likely to <i>hunt</i>	$\eta_{23}(u_*, u^*) = \eta^0 ((1 - u_*) + u^*)$
$\boxed{3} \leftrightarrow \textcircled{2}$	less experienced criminals	$\eta_{32}(u_*, u^*) = \eta^0 (u_* + (1 - u^*))$

Table 1: Non-trivial interactions between a h -particle (represented by a square) with state u_* and a k -particle (represented by a circle) with state u^* .

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Interaction	Qualitative description	μ
$\boxed{2} \leftrightarrow \mathbb{E}_2$	Experienced criminals are more expected to expose themselves	$\mu_2(u_*, \mathbb{E}_2) = \mu^0 u_* - \mathbb{E}_2 $
$\boxed{3} \leftrightarrow \mathbb{E}_3$	Detectives interact with with the mean value through the mean micro-state distance	$\mu_3(u_*, \mathbb{E}_3) = \mu^0 u_* - \mathbb{E}_3 $

Table 2: Non-trivial interactions between a h -candidate particle (represented by a square) with activity u_* and the mean activity value \mathbb{E}_h .



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Parameters involved in the table of games

α_T Susceptibility of citizens to become criminals

α_B Susceptibility of criminals to reach back the state of normal citizen

β Learning dynamics among criminals

γ Motivation/efficacy of security forces to catch criminals

λ Learning dynamics among detectives



Lecture 4 - New Trends in Behavioral Sociology

Case Studies and Trends

Case 1 - Role of the mean wealth

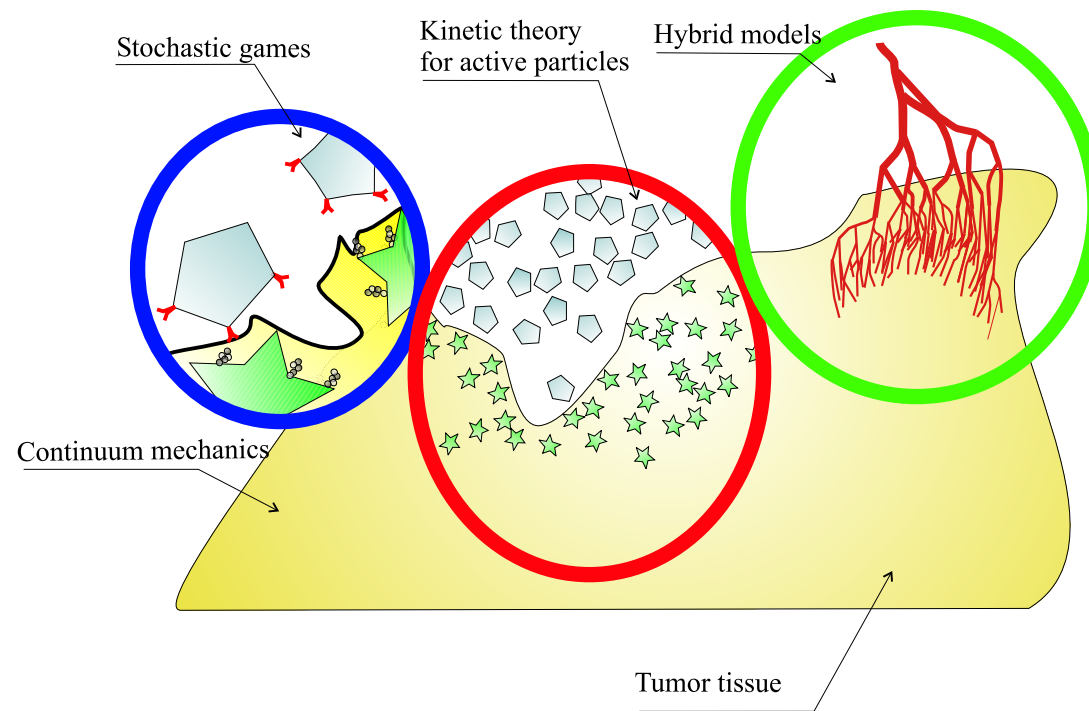
Decreasing mean wealth of the society	\Rightarrow	Increasing number of criminals Increasing criminal ability
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Case 2 - Role of the shape of wealth distribution

Poor society	Equal distribution	\Rightarrow	Slow growth in the number of criminals
	Unequal distribution	\Rightarrow	Fast growth in the number of criminals
Rich society	Equal distribution	\Rightarrow	Fast decrease in the number of criminals
	Unequal distribution	\Rightarrow	Slow decrease in the number of criminals

Lecture 5 - Derivation of Chemotaxis Models

Derivation of Chemotaxis Models





Lecture 5 - Derivation of Chemotaxis Models

The classical Keller and Segel model

$$\begin{cases} \partial_t n = \operatorname{div}_{\mathbf{x}}(D_n(n, S)\nabla_{\mathbf{x}}n - \chi(n, S)n\nabla_{\mathbf{x}}S) + H(n, S), \\ \partial_t S = D_S\Delta S + K(n, S), \end{cases}$$

where $n = n(t, \mathbf{x})$ is the cell (or organism) density at position \mathbf{x} and time t , and $S = S(t, \mathbf{x})$ is the density of the chemoattractant. The terms D_S and D_n are the diffusivity of the chemoattractant and of the cells, respectively. In a more general framework in which diffusions are not isotropic, D_S and D_n could be positive definite matrices.

E.F. Keller and L.A. Segel, Model for chemotaxis, *J. Theor. Biol.*, **30**, (1971), 225-234.

N. Bellomo, A. Bellouquid, Y. Tao, and M. Winkler, On the Theory of Keller-Segel Models, an Overview with Perspectives, *Math. Mod. Meth. Appl. Sci.*, **25** (2015), 1663-1763.



Lecture 5 - Derivation of Chemotaxis Models

Flux limited Keller and Segel models: A nonlinear limited flux that allows a more realistic dynamics: finite speed of propagation c , preservation of fronts in the evolution, or formation of biological patterns. The model collects two of the innovating improved terms consisting in the choice of a flux limited and in the optimal transport.

$$\left\{ \begin{array}{l} \partial_t n = \operatorname{div}_{\mathbf{x}} \left(\frac{n D_n(n, S)}{\sqrt{n^2 + \frac{D_n^2(n, S)}{c^2} |n \nabla_{\mathbf{x}}|^2}} \nabla_{\mathbf{x}} n - \frac{n \chi(n, S)}{\sqrt{1 + |\nabla_{\mathbf{x}} S|^2}} \nabla_{\mathbf{x}} S \right) + H_1(n, S), \\ \partial_t S = \operatorname{div}_{\mathbf{x}} (D_S \cdot \nabla_{\mathbf{x}} S) + H_2(n, S). \end{array} \right.$$

A challenging problem consists in the derivation of the model from the underlying description at the cellular scale and, possibly, a revision of the model itself to avoid unrealistic blow up description of phenomena.



Lecture 5 - Derivation of Chemotaxis Models

Parabolic-Parabolic Scaling

$$\begin{cases} (\partial_t + \mathbf{v} \cdot \nabla_{\mathbf{x}}) f_1 = \nu_1 \mathcal{L}_1[f_1] + \eta_1 \mathcal{G}_1[\mathbf{f}, \mathbf{f}] + \eta_1 \mu_1 \mathcal{I}_1[\mathbf{f}, \mathbf{f}], \\ (\partial_t + \mathbf{v} \cdot \nabla_{\mathbf{x}}) f_2 = \nu_2 \mathcal{L}_2[f_2] + \eta_2 \mathcal{G}_2[\mathbf{f}, \mathbf{f}] + \eta_2 \mu_2 \mathcal{I}_2[\mathbf{f}, \mathbf{f}], \end{cases}$$

$$\mathcal{L}_i[f_i] = \int_{D_{\mathbf{v}}} \left(T_i(\mathbf{v}^* \rightarrow \mathbf{v}) f_i(t, \mathbf{x}, \mathbf{v}^*, u) - T_i(\mathbf{v} \rightarrow \mathbf{v}^*) f_i(t, \mathbf{x}, \mathbf{v}, u) \right) d\mathbf{v}^*,$$

where $T_i(\mathbf{v}^* \rightarrow \mathbf{v})$ is, for the i^{th} subsystem, the probability kernel for the new velocity $\mathbf{v} \in D_{\mathbf{v}}$ assuming that the previous velocity was \mathbf{v}^* .

$$(\varepsilon \partial_t + \mathbf{v} \cdot \nabla_{\mathbf{x}}) f_1^\varepsilon = \frac{1}{\varepsilon^p} \mathcal{L}_1[f_1^\varepsilon] + \varepsilon^q C_1[\mathbf{f}^\varepsilon, \mathbf{f}^\varepsilon] + \varepsilon^{q+r_1} P_1[\mathbf{f}^\varepsilon, \mathbf{f}^\varepsilon],$$

$$(\varepsilon \partial_t + \mathbf{v} \cdot \nabla_{\mathbf{x}}) f_2^\varepsilon = \frac{1}{\varepsilon} \mathcal{L}_2[f_1^\varepsilon](f_2^\varepsilon) + \varepsilon^q \mathcal{G}_2[\mathbf{f}^\varepsilon, \mathbf{f}^\varepsilon] + \varepsilon^{q+r_2} \mathcal{I}_2[\mathbf{f}^\varepsilon, \mathbf{f}^\varepsilon].$$

$p, q \geq 1$, $r_1, r_2 \geq 0$, and ε is a small parameter that is allowed to tend to zero.



Lecture 5 - Derivation of Chemotaxis Models

Assumptions

Assumption H.1. We assume that the turning operator $\mathcal{L}_2[f_2]$ is decomposed as $\mathcal{L}_2[f_2] = \mathcal{L}_2^0[f_2] + \varepsilon \mathcal{L}_2^1[f_1][f_2]$, where \mathcal{L}_2^i , for $i \in \{0, 1\}$, is given by

$$\mathcal{L}_2^i[f_2] = \int_{D_{\mathbf{v}}} \left(T_2^i(\mathbf{v}, \mathbf{v}^*) f_2(t, \mathbf{x}, \mathbf{v}^*, u) - T_2^i(\mathbf{v}^*, \mathbf{v}) f_2(t, \mathbf{x}, \mathbf{v}, u) \right) d\mathbf{v}^*.$$

with $T_2^1 \equiv T_2^1[f_1]$ depending on f_1 and T_2^0 independent on f_1 .

Assumption H.2. We also assume that the turning operators \mathcal{L}_1 and \mathcal{L}_2 satisfy, for all g , the following conditions:

$$\int_{D_{\mathbf{v}}} \mathcal{L}_1[g] d\mathbf{v} = \int_{D_{\mathbf{v}}} \mathcal{L}_2^0[g] d\mathbf{v} = \int_{D_{\mathbf{v}}} \mathcal{L}_2^1[f_1][g] d\mathbf{v} = 0.$$



Lecture 5 - Derivation of Chemotaxis Models

Assumption H.3. There exists a bounded velocity distribution $M_i(\mathbf{v}) > 0$, for $i \in \{1, 2\}$, independent of t, \mathbf{x} , such that the detailed balance

$$T_1(\mathbf{v}, \mathbf{v}^*)M_1(\mathbf{v}^*) = T_1(\mathbf{v}^*, \mathbf{v})M_1(\mathbf{v})$$

$$T_2^0(\mathbf{v}, \mathbf{v}^*)M_2(\mathbf{v}^*) = T_2^0(\mathbf{v}^*, \mathbf{v})M_2(\mathbf{v})$$

Moreover, the flow produced by these equilibrium distributions vanishes, and M_i are normalized, i.e. $\int_{D_{\mathbf{v}}} \mathbf{v} M_i(\mathbf{v}) d\mathbf{v} = 0$ and $\int_{D_{\mathbf{v}}} M_i(\mathbf{v}) d\mathbf{v} = 1$.

Assumption H.4. The kernels $T_1(\mathbf{v}, \mathbf{v}^*)$ and $T_2^0(\mathbf{v}, \mathbf{v}^*)$ are bounded, and there exist constants $\sigma_i > 0$, $i = 1, 2$ such that for all $(\mathbf{v}, \mathbf{v}^*) \in D_{\mathbf{v}} \times D_{\mathbf{v}}$, $\mathbf{x} \in \Omega$:

$$T_1(\mathbf{v}, \mathbf{v}^*) \geq \sigma_1 M_1(\mathbf{v}), \quad T_2^0(\mathbf{v}, \mathbf{v}^*) \geq \sigma_2 M_2(\mathbf{v}),$$



Lecture 5 - Derivation of Chemotaxis Models

Derivation of Keller Segel Models

Letting $L_1 = \mathcal{L}_1$ and $L_2 = \mathcal{L}_2^0$, the above assumptions yields the following:

Lemma

- i) For $f \in L^2$, the equation $L_i[g] = f$, for $i \in \{1, 2\}$, has a unique solution

$$g \in L^2 \left(D_{\mathbf{v}}, \frac{d\mathbf{v}}{M_i} \right),$$

which satisfies

$$\int_{D_{\mathbf{v}}} g(\mathbf{v}) d\mathbf{v} = 0 \quad \text{if and only if} \quad \int_{D_{\mathbf{v}}} f(\mathbf{v}) d\mathbf{v} = 0.$$

- ii) The operator L_i is self-adjoint in the space $L^2 \left(D_{\mathbf{v}}, \frac{d\mathbf{v}}{M_i} \right)$.
- iii) There exists a unique function $\theta_i(\mathbf{v})$ verifying $L_i[\theta_i(\mathbf{v})] = \mathbf{v} M_i(\mathbf{v})$, $i = 1, 2$.
- iv) The kernel of L_i is $N(L_i) = \text{vect}(M_i(\mathbf{v}))$, $i=1,2$.



Lecture 5 - Derivation of Chemotaxis Models

Derivation of Keller Segel Models

Theorem Let $f_i^\varepsilon(t, \mathbf{x}, \mathbf{v}, u)$ be a sequence of solutions to the scaled kinetic system, which verifies Assumptions (H.1.–H.4.) such that f_i^ε converges a.e. in $[0, \infty) \times D_{\mathbf{x}} \times D_{\mathbf{v}} \times D_u$ to a function f_i^0 as ε goes to zero and

$$\sup_{t \geq 0} \int_{D_{\mathbf{x}}} \int_{D_{\mathbf{v}}} \int_{D_u} |f_i^\varepsilon(t, \mathbf{x}, \mathbf{v}, u)|^m du d\mathbf{v} d\mathbf{x} \leq C < \infty$$

for some positive constants $C > 0$ and $m > 2$. Moreover, we assume that the probability kernels \mathcal{B}_{ij} are bounded functions and that the weight functions w_{ij} have finite integrals. It follows that the asymptotic limits f_i^0 is such that n, S are the weak solutions of the following equation (that depends on the values of p, q, r_1 and r_2)

$$\begin{aligned} \partial_t S - \delta_{p,1} \operatorname{div}_{\mathbf{x}} (D_S \cdot \nabla_{\mathbf{x}} S) &= \delta_{q,1} G_1(n, S) + \delta_{q,1} \delta_{r_1,0} I_1(n, S), \\ \partial_t n + \operatorname{div}_{\mathbf{x}} (n \alpha(S) - D_n \cdot \nabla_{\mathbf{x}} n) &= \delta_{q,1} G_2(n, S) + \delta_{q,1} \delta_{r_2,0} I_2(n, S), \end{aligned}$$



Lecture 5 - Derivation of Chemotaxis Models

where $\delta_{a,b}$ stands for the Kronecker delta and D_n, D_S and $\alpha(S)$ are given by

$$D_S = - \int_{D_{\mathbf{v}}} \mathbf{v} \otimes \theta_1(\mathbf{v}) d\mathbf{v}, \quad D_n = - \int_{D_{\mathbf{v}}} \mathbf{v} \otimes \theta_2(\mathbf{v}) d\mathbf{v} \quad (1)$$

and

$$\alpha(S) = - \int_{D_{\mathbf{v}}} \frac{\theta_2(\mathbf{v})}{M_2(\mathbf{v})} \mathcal{L}_2^1[M_1 S](M_2)(\mathbf{v}) d\mathbf{v}, \quad (2)$$

and where, for $i = 1, 2$, G_i and I_i are given by the following:

$$G_i(n, S)(t, \mathbf{x}, u) = \int_{D_{\mathbf{v}}} \mathcal{G}_i \left[\begin{pmatrix} M_1 S \\ M_2 n \end{pmatrix}, \begin{pmatrix} M_1 S \\ M_2 n \end{pmatrix} \right] d\mathbf{v}$$

and

$$I_i(n, S)(t, \mathbf{x}, u) = \int_{D_{\mathbf{v}}} \mathcal{I}_i \left[\begin{pmatrix} M_1 S \\ M_2 n \end{pmatrix}, \begin{pmatrix} M_1 S \\ M_2 n \end{pmatrix} \right] d\mathbf{v}.$$



The End



Thank You!