



On the Difficult Interplay Between Life, “Complexity”, and Mathematical Sciences *Towards a Theory of Complex Living Being*

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Plan of the Lectures

Lecture 1. From Some Reasonings on Complex Systems to a Modeling Strategy

Lecture 2. Two Applications:

2.1 Social Behaviors in Crowds

2.2 System Biology and Immune Competition

Lecture 3. Towards a Mathematical Theory of Living Systems - Looking for the Black Swan

Lecture 1 - Reasonings on Complex Systems

A Personal Bibliographic Search

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Lecture 1 - Reasonings on Complex Systems

- **E. Kant 1790**, da *Critique de la raison pure*, Traduction Française, Press Univ. de France, 1967,

Living Systems: Special structures organized and with the ability to chase a purpose.

- E. Schrödinger, 1943**, *What is Life?*,

I living systems have the ability to extract entropy to keep their own at low levels.

- E.P. Wigner**, *Comm. Pure Appl. Math.*, 1960,

The miracle of the appropriateness of the language of mathematics for the formulation of the laws of physics is a wonderful gift which we neither understand nor deserve.

Lecture 1 - Reasonings on Complex Systems

R. May, *Science* 2003

In the physical sciences, mathematical theory and experimental investigation have always marched together. Mathematics has been less intrusive in the life sciences, possibly because they have been until recently descriptive, lacking the invariance principles and fundamental natural constants of physics.

G. Jona Lasinio, *La Matematica come Linguaggio delle Scienze della Natura*,

Life represents an advanced stage of an evolutive and selective process. It seems to me difficult understanding living entities without considering their historical evolution. Population dynamics is based on a rather primitive mathematical theory, on the other hand it should explain the emergence of individual living entities by selection.

Is life an emerging property of matter?

Lecture 1 - Reasonings on Complex Systems

Hartwell - Nobel Laureate 2001, Nature 1999

- *Biological systems are very different from the physical or chemical systems analyzed by statistical mechanics or hydrodynamics. Statistical mechanics typically deals with systems containing many copies of a few interacting components, whereas cells contain from millions to a few copies of each of thousands of different components, each with very specific interactions.*
- *Although living systems obey the laws of physics and chemistry, the notion of function or purpose differentiates biology from other natural sciences. Organisms exist to reproduce, whereas, outside religious belief rocks and stars have no purpose. Selection for function has produced the living cell, with a unique set of properties which distinguish it from inanimate systems of interacting molecules. Cells exist far from thermal equilibrium by harvesting energy from their environment.*

Lecture 1 - Reasonings on Complex Systems

N.B. H. Berestycki, F. Brezzi, and J.P. Nadal, *Mathematics and Complexity in Life and Human Sciences*, Mathematical Models and Methods in Applied Sciences, 2010.

The study of complex systems, namely systems of many individuals interacting in a non-linear manner, has received in recent years a remarkable increase of interest among applied mathematicians, physicists as well as researchers in various other fields as economy or social sciences.

Their collective overall behavior is determined by the dynamics of their interactions. On the other hand, a traditional modeling of individual dynamics does not lead in a straightforward way to a mathematical description of collective emerging behaviors.

In particular it is very difficult to understand and model these systems based on the sole description of the dynamics and interactions of a few individual entities localized in space and time.

Lecture 1 - Reasonings on Complex Systems

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. These can be expressed without the application of any external organizing principle. They typically operate *out-of-equilibrium*. *For example, a constant struggle with the environment is developed to remain in a particular out-of-equilibrium state, namely stay alive.*

2. Heterogeneity: The ability to express a strategy is not the same for all entities: *Heterogeneity* characterizes a great part of living systems, namely, the characteristics of interacting entities can even differ from an entity to another belonging to the same structure. *In developmental biology, this is due to different phenotype expressions generated by the same genotype.*

3. Learning ability: Living systems receive inputs from their environments and have the ability to learn from past experience. Therefore their strategic ability and the characteristics of interactions evolve in time. *Societies can induce a collective strategy toward individual learning.*

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4. *Nonlinear Interactions:* Interactions are nonlinearly additive and involve immediate neighbors, but in some cases also distant particles. Living systems have the ability to communicate and can possibly choose different observation paths. In some cases, the topological distribution of a fixed number of neighbors can play a prominent role in the development of the strategy and interactions. Living entities *play a game at each interaction* with an output that is technically related to their strategy often related to surviving and adaptation ability. *Individual interactions in swarms can depend on the number of interacting entities rather than on their distance.*

5. *Darwinian selection and time as a key variable:* All living systems are evolutionary. Birth processes can generate individuals more fitted to the environment, who can generate new individuals again more fitted to the outer environment. Neglecting this aspect means that the time scale of observation and modeling of the system itself is not long enough to observe evolutionary events. The time scale can be very short for cellular systems and very long for vertebrates. *Micro-Darwinian occurs at small scales, while Darwinian evolution is generally interpreted at large scales.*

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Technical Features of Complex Systems

- ***Multiscale aspects:*** The study of complex living systems always needs a *multiscale approach*, such that the dynamics at the large scale needs to be properly related to the dynamics at the low scales. For instance, the functions expressed by a cell are determined by the dynamics at the molecular (genetic) level. This feature characterizes also the dynamics of vehicles and animals, where the mechanical system is linked to individual behaviors. In any case, macroscopic models generally kill the heterogeneous behaviors exhibited at the low scales.
- ***Time varying role of the environment:*** The environment surrounding a living system evolves in time, also due to the interaction with the inner system. Therefore the output of this interaction evolves in time. One of the several implications is that the number of components of a living system might change in time.

Lecture 1 - Reasonings on Complex Systems

On the Interpretation of Empirical Data

The collective dynamics of complex systems is determined by interactions at the micro-scale ruled by the strategy that interacting entities are able to express. This collective dynamics exhibits emerging behaviors as well as some aspects of the dynamics which may not be specifically related to complexity, such as steady conditions uniform in space that are reproduced in analogy with classical systems. These considerations lead to state that models should have the ability to depict both emerging behaviors far from steady cases, which should not be artificially imposed in the structure of the model, rather should be induced by interactions at the micro-scale.

Accordingly, empirical data should be used toward the assessment of models at the micro-scale. Subsequently validation of models should be obtained by investigating their ability to depict emerging behaviors. However, the process can be implemented if the modeling at the micro-scale is consistent with the physics of the real system, and if the tuning method leads to a unique solution of the inverse problem of parameters identification.

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What is the Black Swan? It is worth detailing a little more the expression *Black Swan*, introduced in the specialized literature for indicating unpredictable events, which are far away from those generally observed by repeated empirical evidence. According to the definition by Taleb a Black Swan is specifically characterized as follows:

“A Black Swan is a highly improbable event with three principal characteristics: It is unpredictable; it carries a massive impact; and, after the fact, we concoct an explanation that makes it appear less random, and more predictable, than it was.”

N. N. Taleb, *The Black Swan: The Impact of the Highly Improbable*, Random House, New York City, 2007.

Since it is very difficult to predict directly the onset of a black swan, it is useful looking for *the presence of early signals*

M. Scheffer, J. Bascompte, W. A. Brock, V. Brovkin, S. R. Carpenter, V. Dakos, H. Held, E. H. van Nes, M. Rietkerk, and G. Sugihara, Early-warning signals for critical transitions, *Nature*, 461, 53–59, (2009).

Lecture 1 - Reasonings on Complex Systems

Complexity Features in the Metamorphosis by Escher



Heterogeneous ability to express a strategy

Nonlinear Interactions

Learning ability

Darwinian selection and time as a key variable

Complexity in the interpretation of reality

The Black Swan.

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To what extent the Metamorphosis represents the complexity of living systems?

Let us leave some freedom to our fantasy by taking the liberty to look at the fascinating piece of art and concentrate to the right hand-end part where the landscape evolves in time going first from a geometrical village made of similarly looking houses to a real village with a heterogeneous distribution of houses' shape. Escher's representations have greatly attracted the fantasy of mathematicians who, consciously or not, have linked them to some mathematical reasonings. This is precisely what it is here suggested by posing the question in the title of the slide.

The evolution is related to interactions, definitely multiple ones. Is nonlinearity somehow expressed? the evolution is selective as shown by the transition from essential shapes to an organized village, where all available spaces are well exploited. Moreover, the presence of a church, that takes an important part of the space and a somehow central position, indicates the presence of a cultural evolution. This latter might even reflect a multiscale dynamics. In fact, it results as the output of the action from the micro-scale of individuals to the macro-scale of the village.

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Suddenly the landscape changes from a village, turning into a chess plate, the only connections being a Bridge and a tower. Can this sudden change be interpreted as a “Black Swan”?

The real Tower is not that of the chess plate, however, it can be interpreted as an early signal that an extreme event is going to happen. In any case, the various changes in the picture can be interpreted as predictable emerging behaviors, while the last one is not a predictable event. One might consider that Escher went through the experience of two world wars, while a peaceful village is transformed into a battle between the two armies of the chess plate.

Since the village exists in reality (it is in the Mediterranean coast immediately on the South of the village of Amalfi) does the Tower truly exist? The village looks at the sea, while the tower cannot be observed looking at it from the front as in the picture. On the other hand, looking at it from the rear it is possible to observe a tower on the cape in front of the village. This is not sufficient to answer the question posed above; however one can realize that emerging behaviors are also difficult to be interpreted.

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Strategy Step I

- The mathematical approach devoted to the ambitious aim of understanding the essence of life and evolution and, consequently, of describing by mathematical equations the dynamics of living systems, cannot be based on classical field theories as usual in the modeling of inert matter.
- Accordingly, one can either look for **heuristic models** based on a purely phenomenological interpretation of the system under consideration, or look for **mathematical models** derived within suitable mathematical structures consistent with the paradigms of complexity.
- This second approach is, according to the authors's bias, more rigorous and is, in any case the necessary step towards the development of a self-consistent theory linking mathematics to the specific science under consideration, say biology, economy, sociology, etcetera. In other words, the structure offers the mathematical theory, while the characterization of the interactions at the micro-scale should be delivered by theoretical tools of the other science.

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Strategy Step II

- Understanding the links between the dynamics of living systems and their complexity features;
- Derivation a general mathematical structure, consistent with the aforesaid features, with the aim of offering the conceptual framework toward the derivation of specific models;
- Design of specific models corresponding to well defined classes of systems by implementing the said structure with suitable model of individual-based interactions according to a detailed interpretation of the dynamics at the micro-scale;
- Validation of models by comparison of the dynamics predicted by them with that one resulting from empirical data;
- Analysis of the gap between modeling and mathematical theory.

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Strategy Step III

- The overall system is subdivided into *functional subsystems* constituted by entities, called *active particles*, whose individual state is called *activity*;
- The state of each functional subsystem is defined by a suitable, time dependent, probability distribution over the microscopic state, which includes position, velocity, and activity variables, which represent the strategies expressed heterogeneously by each individual;
- Interactions are modeled by games, more precisely stochastic games, where the state of the interacting particles and the output of the interactions are known in probability;
- The evolution of the probability distribution is obtained by a balance of particles within elementary volume of the space of the microscopic states, where the dynamics of inflow and outflow of particles is related to interactions at the microscopic scale.

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Representation for space distributed systems in each node

Consider active particles in a node for functional subsystems labeled by the subscript i .

- The description of the overall state of the system is delivered by the *generalized 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 subsystem.

- $\mathbf{w} = \{\mathbf{x}, \mathbf{v}, u\}$ is an element of the *space of the microscopic states*.
- \mathbf{x} and \mathbf{v} Represent the *mechanical variables*, whenever these have a physical meaning: in some cases they are vanishing variables, while in networks, the space is substituted by nodes.
- The *activity variable* can be a vector.

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- The *activity terms* are computed as follows:

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

is the *local activation*, while the *local activation density* is given by:

$$ad_i[f_i](t, \mathbf{x}) = \frac{a_j[f_i](t, \mathbf{x})}{\nu_i[f_i](t, \mathbf{x})} = \frac{1}{\nu_i[f_i](t, \mathbf{x})} \int_{D_{\mathbf{v}} \times D_u} u f_i(t, \mathbf{x}, \mathbf{v}, u) d\mathbf{v} du .$$

- More in general one can introduce higher order moments for the activation:

$$a_i^p[f_i](t, \mathbf{x}) = \int_{D_{\mathbf{v}} \times D_u} u^p f_i(t, \mathbf{x}, \mathbf{v}, u) d\mathbf{v} du ,$$

- *Mechanical terms* are computed analogously and depend on the activity terms.

For instance the *local densities* are computed as follows:

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

and similarly for higher order quantities.

Lecture 1 - Reasonings on Complex Systems

Stochastic Games Living entities, at each interaction, *play a game* with an output that technically depends on their strategy often related to surviving and adaptation abilities, namely to an individual or collective search for fitness. The output of the game generally is not deterministic even when a causality principle is identified.

- **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 $f_h = f_h(t, \mathbf{x}_*, \mathbf{v}_*, u_*) = f_h(t, \mathbf{w}_*)$.

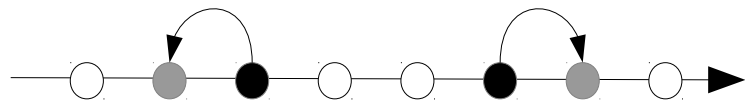
Lecture 1 - Reasonings on Complex Systems

Stochastic Games

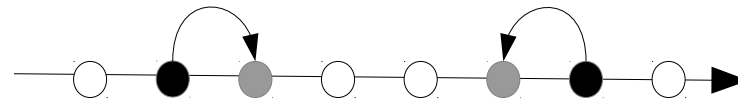
1. **Competitive (dissent):** When one of the interacting particle increases its status by taking advantage of the other, obliging the latter to decrease it. Therefore the competition brings advantage to only one of the two. This type of interaction has the effect of increasing the difference between the states of interacting particles, due to a kind of driving back effect.
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. Such type of interaction leads to a decrease of the difference between the interacting particles' states, due to a sort of dragging effect.
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 - Reasonings on Complex Systems

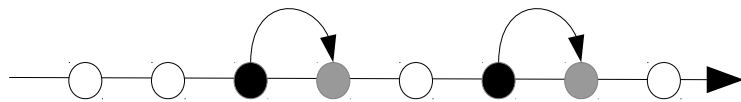
Stochastic Games Pictorial illustration of (a) competitive, (b) cooperative, (c) hiding-chasing and (d) learning game dynamics between two active particles. Black and grey bullets denote, respectively, the pre- and post-interaction states of the particles.



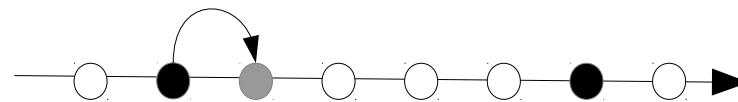
(a) Competition



(b) Cooperation



(c) Hiding-chasing



(d) Learning

Lecture 1 - Reasonings on Complex Systems

Stochastic Games

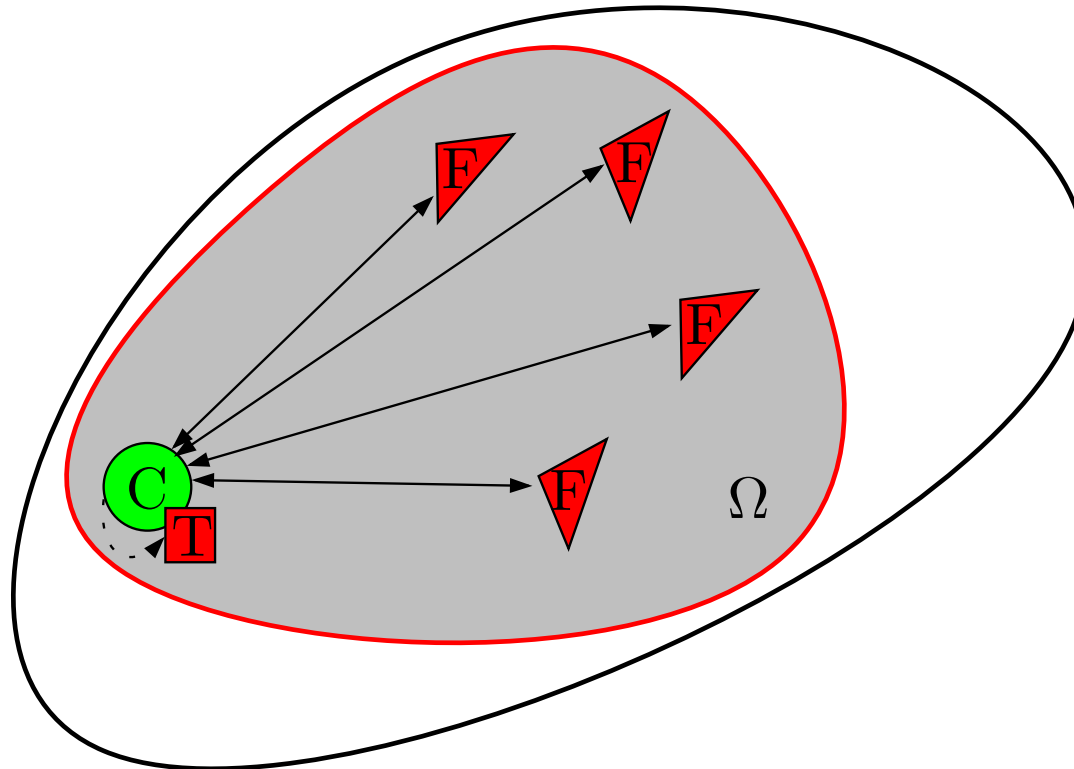
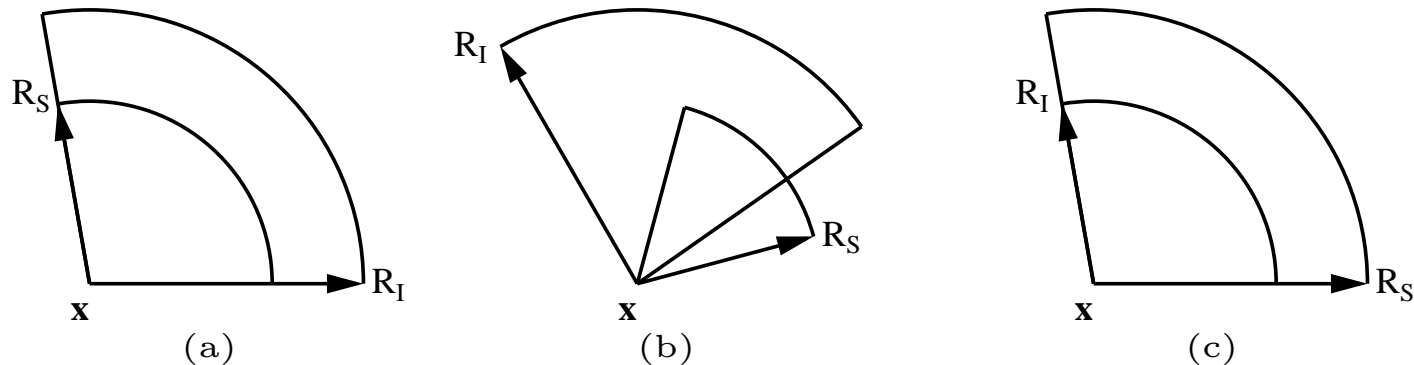
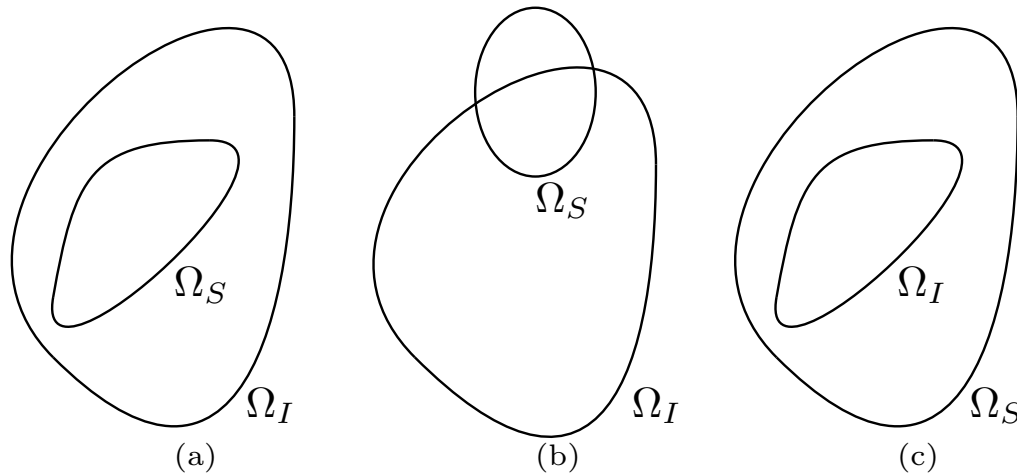


Figure 1: – Active particles interact with other particles in their action domain

Lecture 1 - Reasonings on Complex Systems

Stochastic Games On the interplay between sensitivity and interaction domain



Lecture 1 - Reasonings on Complex Systems

Stochastic Games

Interactions with modification of activity and transition: Generation of particles into a new functional subsystem occurs through pathways. Different paths can be chosen according to the dynamics at the lower scale.

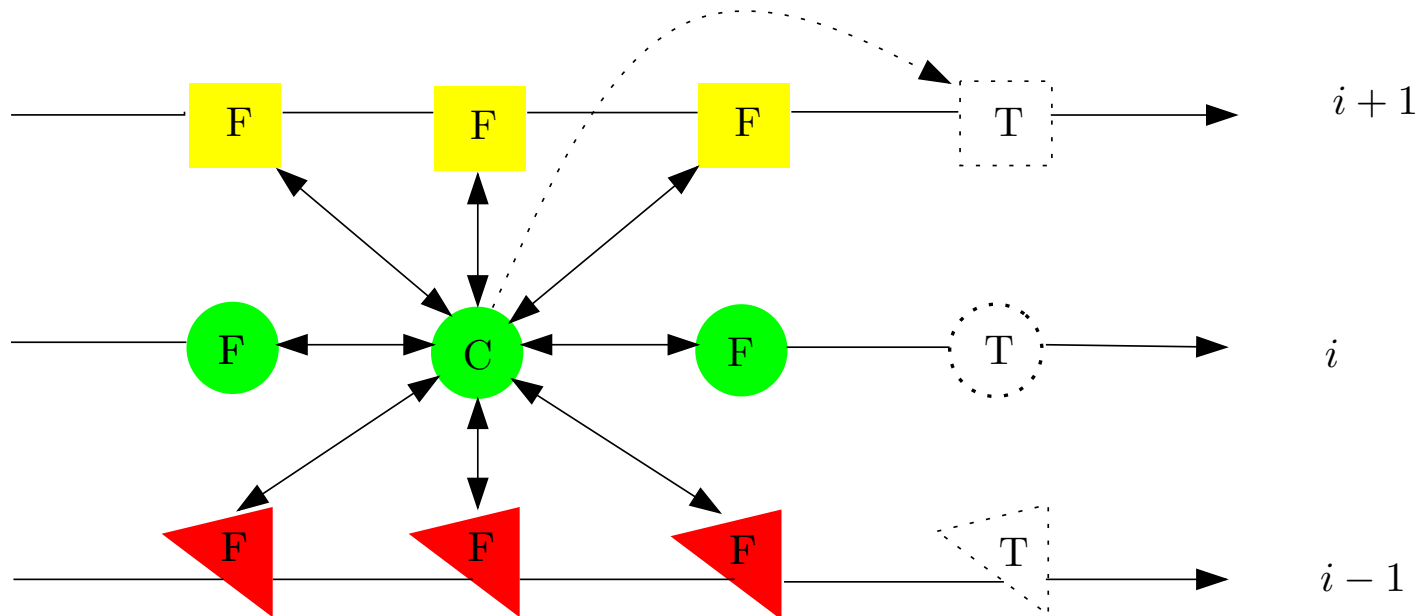


Figure 2: – Active particles during proliferation move from one functional subsystem to the other through pathways.

Plan of the Lectures

Lecture 1. From Some Reasonings on Complex Systems to a Modeling Strategy

Lecture 2. Two Applications:

2.1 Social Behaviors in Crowds

2.2 System Biology and Immune Competition

Lecture 3. Towards a Mathematical Theory of Living Systems

Lecture 2 - Social Behaviors in Crowds



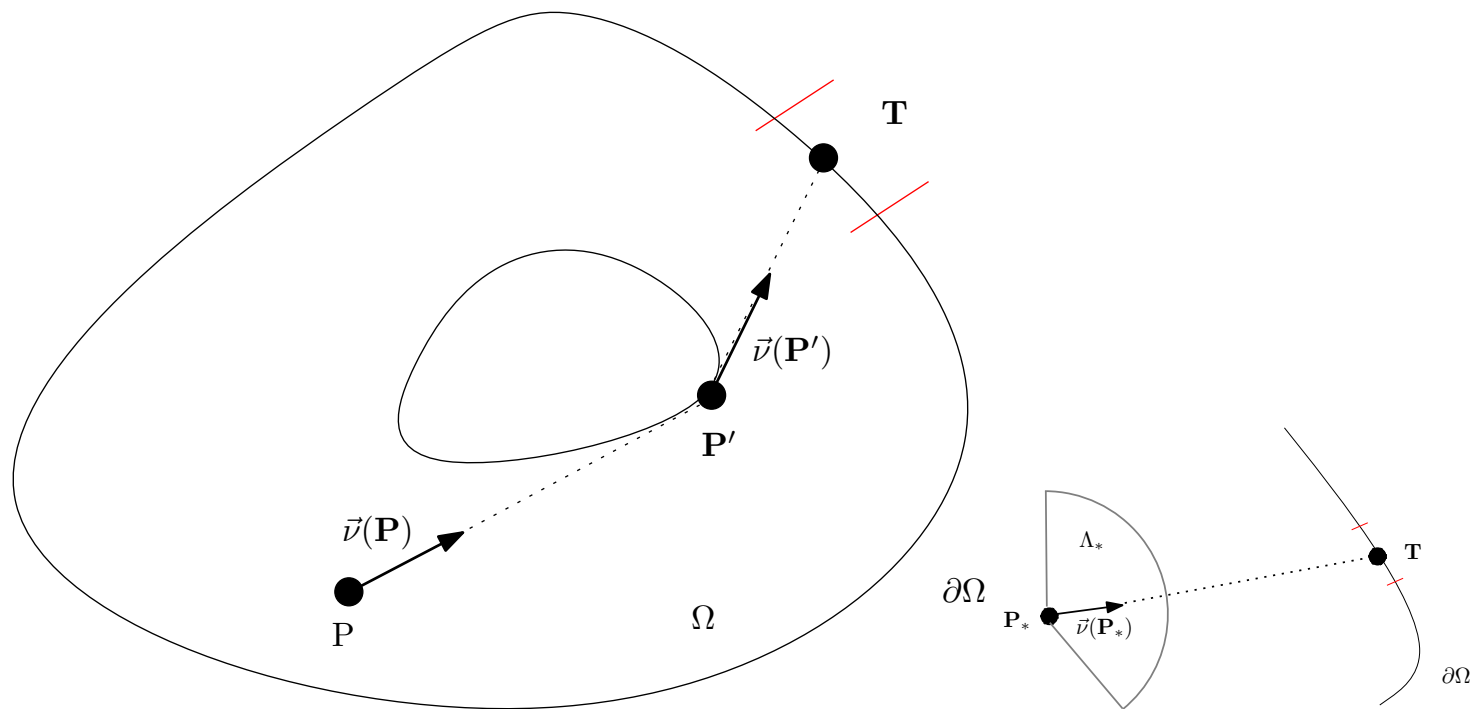
Lecture 2 - 2.1 Social Behaviors in Crowds

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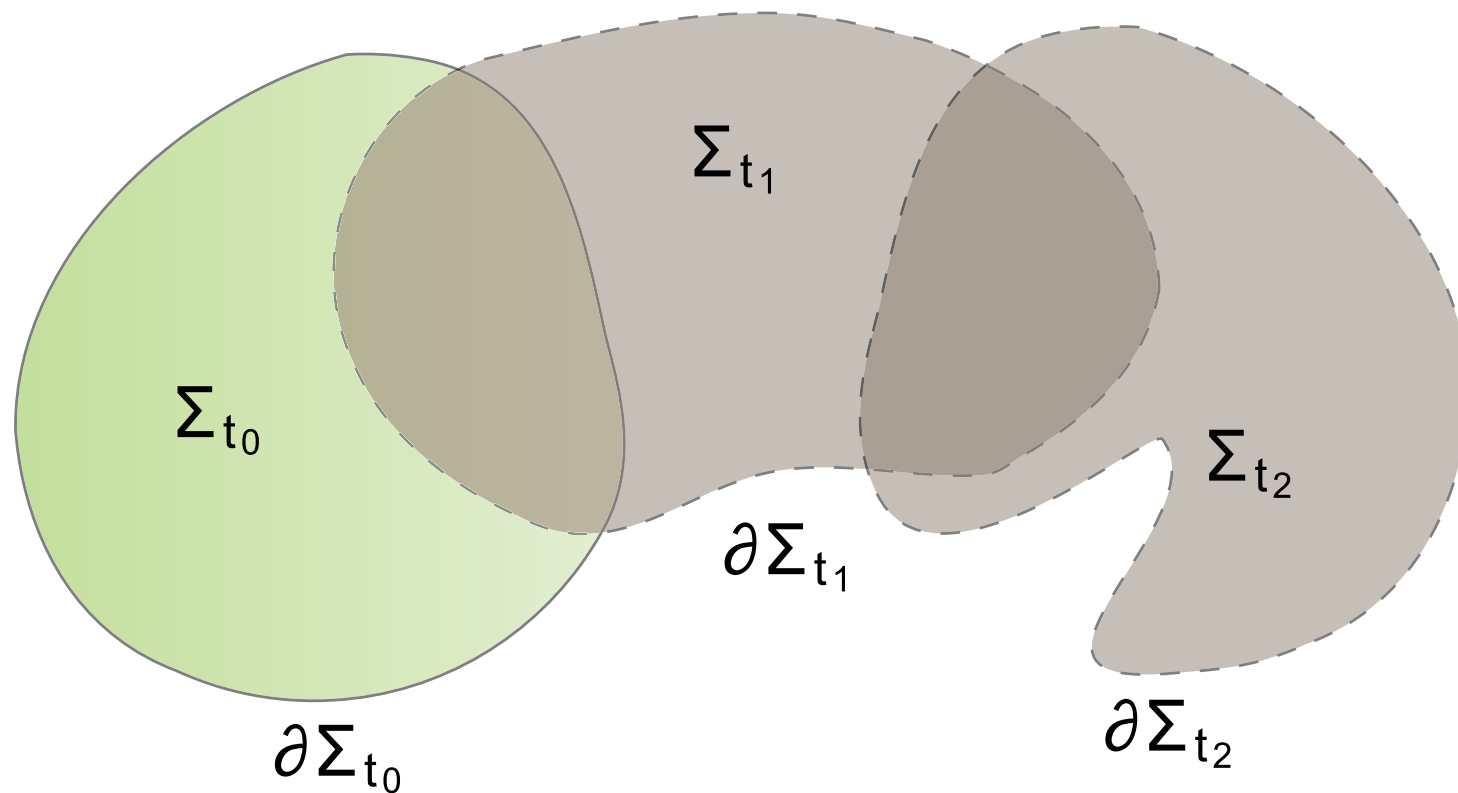
Lecture 2 - 2.1 Social Behaviors in Crowds

Crowds in Bounded Domain with Obstacles



Lecture 2 - 2.1 Social Behaviors in Crowds

Crowds in unbounded Domains



Lecture 2 - 2.1 Social Behaviors in Crowds

Active particles and micro-scale states

Crowd dynamics	
Active particles	Pedestrians
Microscopic state	Position
	Velocity
	Activity
Functional subsystems	Different abilities
	Individuals pursuing different targets etc.

Lecture 2 - 2.1 Social Behaviors in Crowds

Polar coordinates with discrete values are used for the velocity variable $\mathbf{v} = \{v, \theta\}$:

$$I_\theta = \{\theta_1 = 0, \dots, \theta_i, \dots, \theta_n = \frac{n}{n-1} 2\pi\}, \quad I_v = \{v_1 = 0, \dots, v_j, \dots, v_m = 1\}.$$

$$f(t, \mathbf{x}, \mathbf{v}, u) = \sum_{i=1}^n \sum_{j=1}^m f_{ij}(t, \mathbf{x}, u) \delta(\theta - \theta_i) \otimes \delta(v - v_j).$$

Some specific cases can be considered. For instance the case of two different groups, labeled with the superscript $\sigma = 1, 2$, which move towards two different targets.

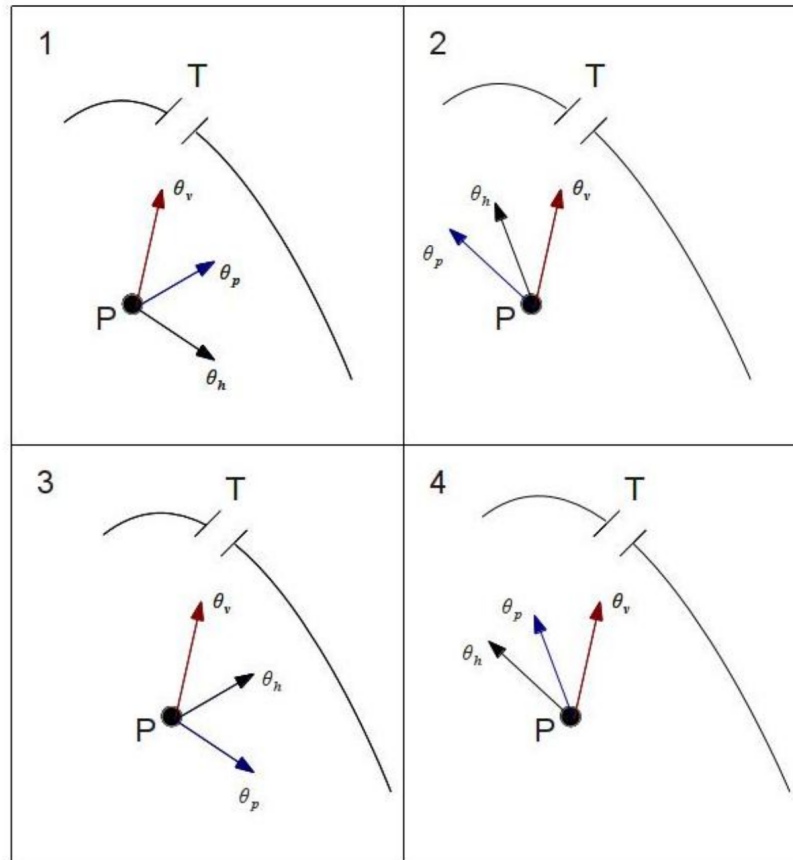
$$f^\sigma(t, \mathbf{x}, \mathbf{v}, u) = \sum_{i=1}^n \sum_{j=1}^m f_{ij}^\sigma(t, \mathbf{x}) \delta(\theta - \theta_i) \otimes \delta(v - v_j) \otimes \delta(u - u_0),$$

where $f_{ij}^\sigma(t, \mathbf{x}) = f(t, \mathbf{x}, \theta_i, v_j)$ corresponding, for each group $\sigma = 1, 2$, to the ij -particle, namely to the pedestrian moving in the direction θ_i with velocity v_j .

$$\rho(t, \mathbf{x}) = \sum_{\sigma=1}^2 \rho^\sigma(t, \mathbf{x}) = \sum_{\sigma=1}^2 \sum_{i=1}^n \sum_{j=1}^m f_{ij}^\sigma(t, \mathbf{x}),$$

Lecture 2 - 2.1 Social Behaviors in Crowds

Interactions in the table of games



Particle in P moves to a direction θ_h (black arrow) and interacts with a field particle moving to θ_p (blue arrow), the direction to the target is θ_v (red arrow).

Lecture 2 - 2.1 Social Behaviors in Crowds

$$\begin{aligned}
 (\partial_t + \mathbf{v}_{ij} \cdot \partial_{\mathbf{x}}) f_{ij}^\sigma(t, \mathbf{x}) &= \mathcal{J}[\mathbf{f}](t, \mathbf{x}) \\
 &= \sum_{h,p=1}^n \sum_{k,q=1}^m \int_{\Lambda} \eta[\rho(t, \mathbf{x}^*)] \mathcal{A}_{hk,pq}^\sigma(ij) [\rho(t, \mathbf{x}^*)] f_{hk}^\sigma(t, \mathbf{x}) f_{pq}^\sigma(t, \mathbf{x}^*) d\mathbf{x}^* \\
 &- f_{ij}^\sigma(t, \mathbf{x}) \sum_{p=1}^n \sum_{q=1}^m \int_{\Lambda} \eta[\rho(t, \mathbf{x}^*)] f_{pq}^\sigma(t, \mathbf{x}^*) d\mathbf{x}^*,
 \end{aligned}$$

where $\mathbf{f} = \{f_{ij}\}$, while the term $\mathcal{A}_{hk,pq}^\sigma(ij)$ should be consistent with the probability density property:

$$\sum_{i=1}^n \sum_{j=1}^m \mathcal{A}_{hk,pq}^\sigma(ij) = 1, \quad \forall hp \in \{1, \dots, n\}, \quad \forall kq \in \{1, \dots, m\},$$

for $\sigma = 1, 2$, and for all conditioning local density.

Pedestrians have a visibility zone $\Lambda = \Lambda(\mathbf{x})$, which does not coincide with the whole domain Ω due to the limited visibility angle of each individual.

Lecture 2 - 2.1 Social Behaviors in Crowds

- **Interaction rate:**

$$\eta(\rho(t, \mathbf{x})) = \eta^0(1 + \rho(t, \mathbf{x})).$$

- **Transition probability density:** The approach proposed here is based on the assumption that particles are subject to three different influences, namely the *trend to the exit point*, the *influence of the stream* induced by the other pedestrians, and the selection of the path with minimal density gradient. A simplified interpretation of the phenomenological behavior is obtained by assuming the factorization of the two probability densities modeling the modifications of the velocity direction and modulus:

$$\mathcal{A}_{hk,pq}^\sigma(ij) = \mathcal{B}_{hp}^\sigma(i)(\theta_h \rightarrow \theta_i | \rho(t, \mathbf{x})) \times \mathcal{C}_{kq}^\sigma(j)(v_k \rightarrow v_j | \rho(t, \mathbf{x})).$$

– *Interaction with a upper stream and target directions, namely $\theta_p > \theta_h$, $\theta_v > \theta_h$:*

$$\mathcal{B}_{hp}^\sigma(i) = \alpha u_0(1 - \rho) + \alpha u_0 \rho \quad \text{if } i = h + 1,$$

$$\mathcal{B}_{hp}^\sigma(i) = 1 - \alpha u_0(1 - \rho) - \alpha u_0 \rho \quad \text{if } i = h,$$

$$\mathcal{B}_{hp}^\sigma(i) = 0 \quad \text{if } i = h - 1.$$

Lecture 2 - 2.1 Social Behaviors in Crowds

– Interaction with a upper stream and low target direction $\theta_p > \theta_h$; $\theta_v < \theta_h$:

$$\mathcal{B}_{hp}^\sigma(i) = \alpha u_0 \rho \quad \text{if } i = h + 1,$$

$$\mathcal{B}_{hp}^\sigma(i) = 1 - \alpha u_0(1 - \rho) - \alpha u_0 \rho \quad \text{if } i = h,$$

$$\mathcal{B}_{hp}^\sigma(i) = \alpha u_0 (1 - \rho) \quad \text{if } i = h - 1.$$

– Interaction with a lower stream and upper target direction $\theta_p < \theta_h$; $\theta_v > \theta_h$:

$$\mathcal{B}_{hp}^\sigma(i) = \alpha u_0(1 - \rho) \quad \text{if } i = h + 1,$$

$$\mathcal{B}_{hp}^\sigma(i) = 1 - \alpha u_0(1 - \rho) - \alpha u_0 \rho \quad \text{if } i = h,$$

$$\mathcal{B}_{hp}^\sigma(i) = \alpha u_0 \rho \quad \text{if } i = h - 1.$$

– Interaction with a lower stream and target directions $\theta_p < \theta_h$; $\theta_v < \theta_h$:

$$\mathcal{B}_{hp}^\sigma(i) = 0 \quad \text{if } i = h + 1,$$

$$\mathcal{B}_{hp}^\sigma(i) = 1 - \alpha u_0(1 - \rho) - \alpha u_0 \rho \quad \text{if } i = h,$$

$$\mathcal{B}_{hp}^\sigma(i) = \alpha u_0 (1 - \rho) + \alpha u_0 \rho \quad \text{if } i = h - 1.$$

Lecture 2 - 2.1 Social Behaviors in Crowds

– Interaction with faster particles $v_k < v_q$ and slower particles $v_k > v_q$

$$C_{kq}^\sigma(j) = \begin{cases} 1 - \beta u_0 \rho, & j = k; \\ \beta u_0 \rho, & j = k + 1; \\ 0, & \text{otherwise.} \end{cases} \quad C_{kq}^\sigma(j) = \begin{cases} \beta u_0 \rho, & j = k; \\ 1 - \beta u_0 \rho, & j = k - 1; \\ 0, & \text{otherwise.} \end{cases}$$

– Interaction with equal velocity particles $v_k = v_q$

$$C_{kq}^\sigma(j) = \begin{cases} 1 - 2\beta u_0 \rho, & j = k; \\ \beta u_0 \rho, & j = k - 1; \\ \beta u_0 \rho, & j = k + 1. \end{cases}$$

– for $k = 1$ the candidate particle cannot reduce velocity, while for $k = k$ cannot increase it:

$$C_{kq}^\sigma(j) = \begin{cases} 1 - \beta u_0 \rho, & j = 1; \\ \beta u_0 \rho, & j = 2; \\ 0, & \text{otherwise;} \end{cases} \quad C_{kq}^\sigma(j) = \begin{cases} \beta u_0 \rho, & j = m - 1; \\ 1 - \beta u_0 \rho, & j = m; \\ 0, & \text{otherwise.} \end{cases}$$

Lecture 2 - 2.1 Social Behaviors in Crowds

Mild form of the initial value problem

$$\widehat{f}_{ij}^{\sigma}(t, \mathbf{x}) = \phi_{ij}^{\sigma}(\mathbf{x}) + \int_0^t \left(\widehat{\Gamma}_{ij}^{\sigma}[\mathbf{f}, \mathbf{f}](s, \mathbf{x}) - \widehat{f}_{ij}^{\sigma}(s, \mathbf{x}) \widehat{\mathcal{L}}[\mathbf{f}](s, \mathbf{x}) \right) ds,$$
$$i \in \{1, \dots, n\}, \quad j \in \{1, \dots, m\}, \quad \sigma \in \{1, 2\},$$

where the following notation has been used for any given vector $f(t, \mathbf{x})$:

$$\widehat{f}_{ij}^{\sigma}(t, \mathbf{x}) = f_{ij}^{\sigma}(t, x + v_j \cos(\theta_i)t, y + v_j \sin(\theta_i)t).$$

H.1. For all positive R , there exists a constant $C_{\eta} > 0$ so that

$$0 < \eta(\rho) \leq C_{\eta}, \quad \text{whenever } 0 \leq \rho \leq R.$$

H.2. Both the encounter rate $\eta[\rho]$ and the transition probability $\mathcal{A}_{hk,pq}^{\sigma}(ij)[\rho]$ are Lipschitz continuous functions of the macroscopic density ρ , i.e., that there exist constants $L_{\eta}, L_{\mathcal{A}}$ is such that

$$| \eta[\rho_1] - \eta[\rho_2] | \leq L_{\eta} | \rho_1 - \rho_2 |, \quad | \mathcal{A}_{hk,pq}^{\sigma}(ij)[\rho_1] - \mathcal{A}_{hk,pq}^{\sigma}(ij)[\rho_2] | \leq L_{\mathcal{A}} | \rho_1 - \rho_2 |$$

whenever $0 \leq \rho_1 \leq R, 0 \leq \rho_2 \leq R$, and all $i, h, p = 1, \dots, n$ and $j, k, q = 1, \dots, m$.

Lecture 2 - 2.1 Social Behaviors in Crowds

Existence Theory

THEOREM: Let $\phi_{ij}^\sigma \in L_\infty \cap L^1$, $\phi_{ij}^\sigma \geq 0$, then there exists ϕ^0 so that, if $\|\phi\|_1 \leq \phi^0$, there exist T , a_0 , and R so that a unique non-negative solution to the initial value problem exists and satisfies:

$$f \in X_T, \quad \sup_{t \in [0, T]} \|f(t)\|_1 \leq a_0 \|\phi\|_1,$$

$$\rho(t, \mathbf{x}) \leq R, \quad \forall t \in [0, T], \quad \mathbf{x} \in \Omega.$$

Moreover, if $\sum_{\sigma=1}^2 \sum_{i=1}^n \sum_{j=1}^m \|\phi_{ij}^\sigma\|_\infty \leq 1$, and $\|\phi\|_1$ is small, one has $\rho(t, \mathbf{x}) \leq 1$, $\forall t \in [0, T]$, $\mathbf{x} \in \Omega$.

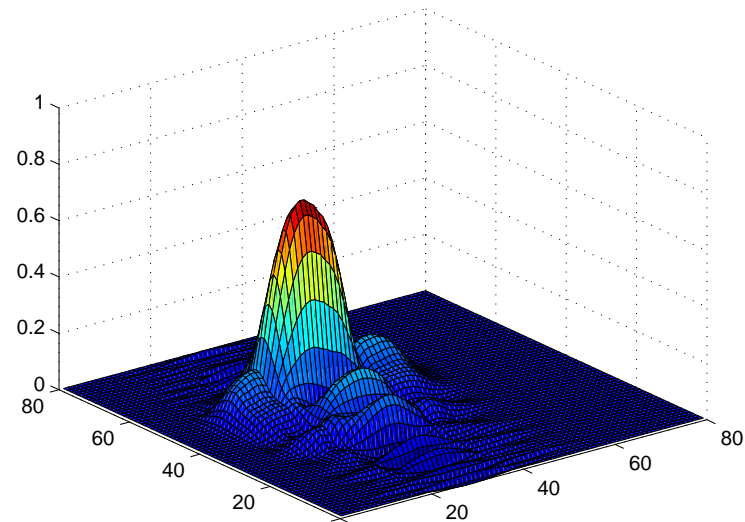
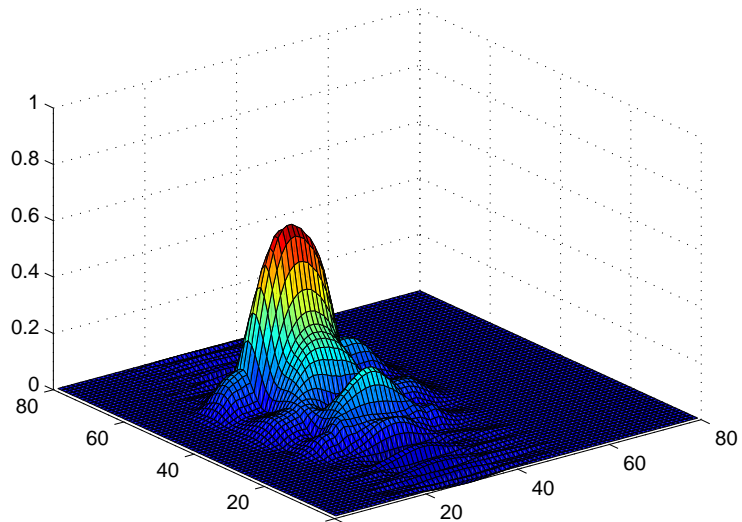
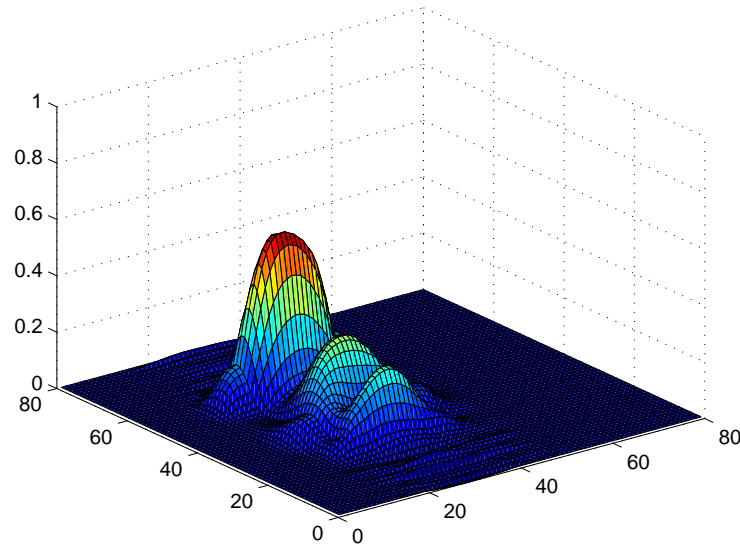
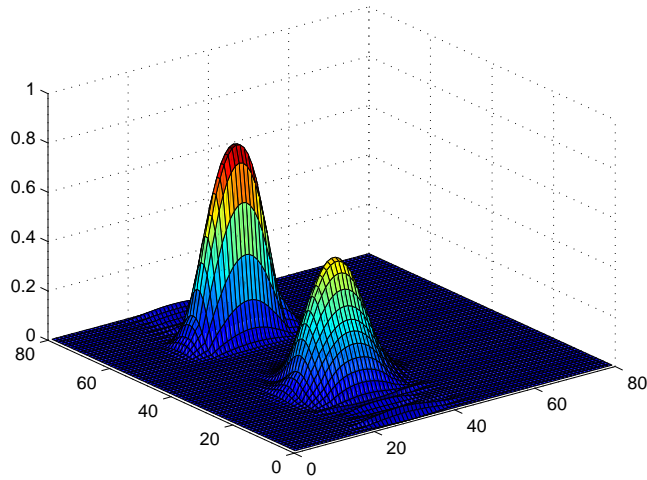
There exist ϕ^r , ($r = 1, \dots, p-1$) such that if $\|\phi\|_1 \leq \phi^r$, there exists a_r so that it is possible to find a unique non-negative solution to the initial value problem satisfying for any $r \leq p-1$ the following $f(t) \in X[0, (p-1)T]$,

$$\sup_{t \in [0, T]} \|f(t + (r-1)T)\|_1 \leq a_{r-1} \|\phi\|_1,$$

and $\rho(t + (r-1)T, \mathbf{x}) \leq R$, $\forall t \in [0, T]$, $\mathbf{x} \in \Omega$. Moreover, $\rho(t + (r-1)T, \mathbf{x}) \leq 1$, $\forall t \in [0, T]$, $\mathbf{x} \in \Omega$.

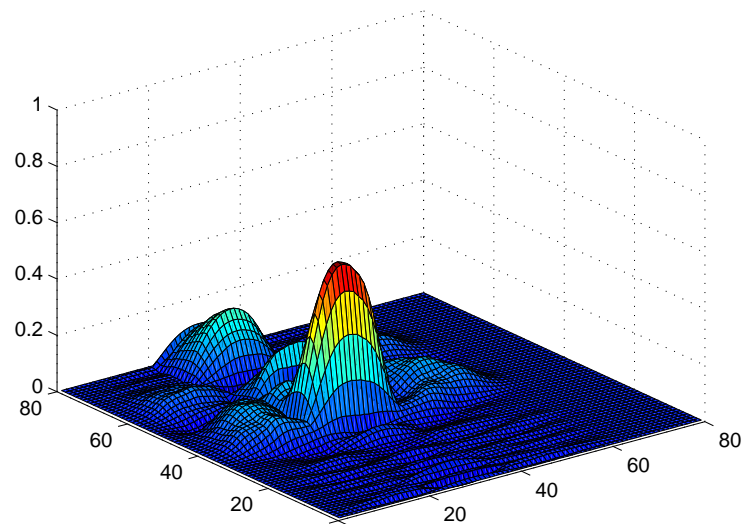
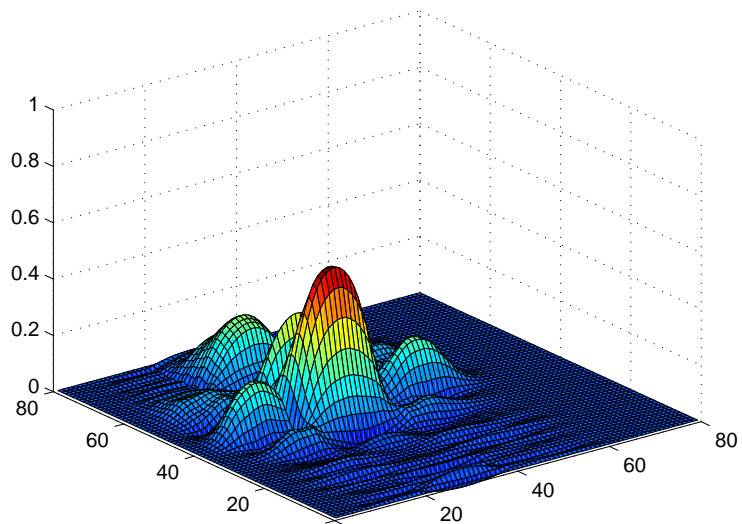
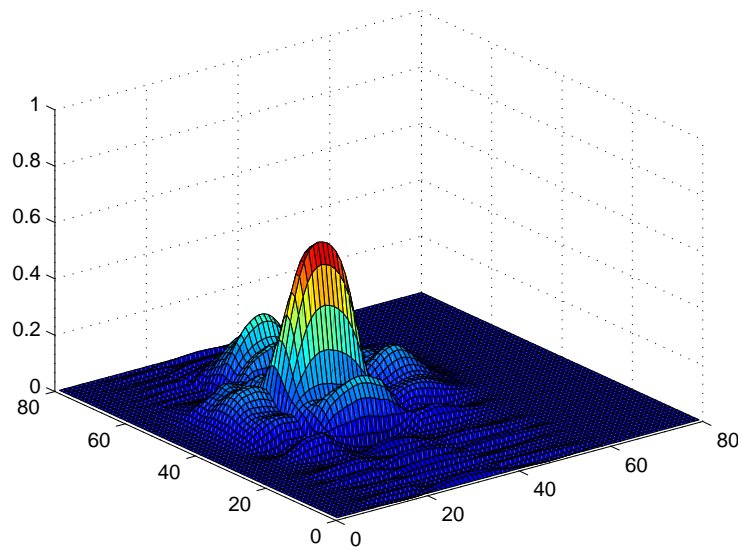
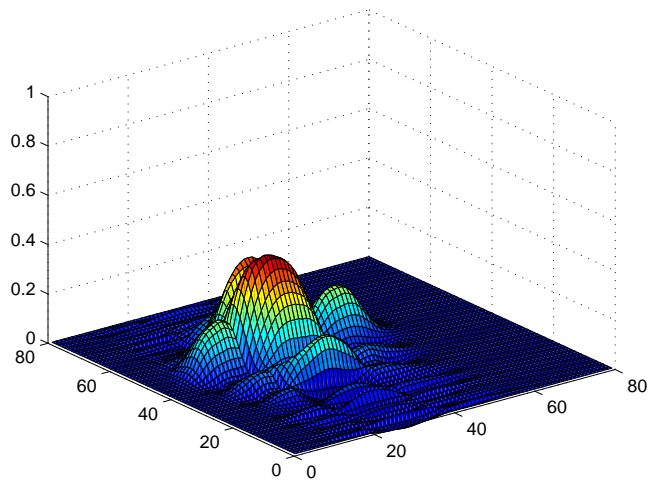
Lecture 2 - 2.1 Social Behaviors in Crowds

A Case Study



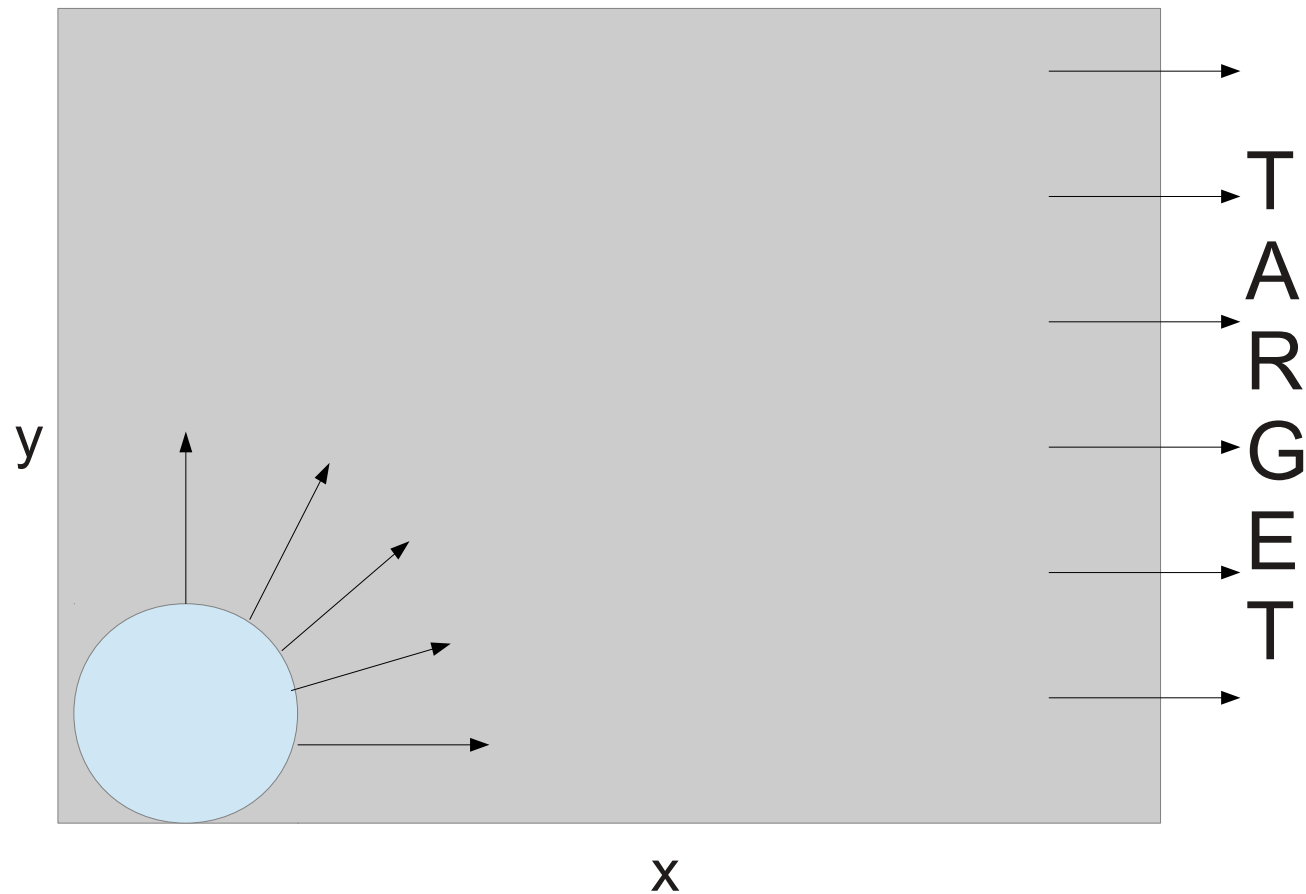
Lecture 2 - 2.1 Social Behaviors in Crowds

A Case Study

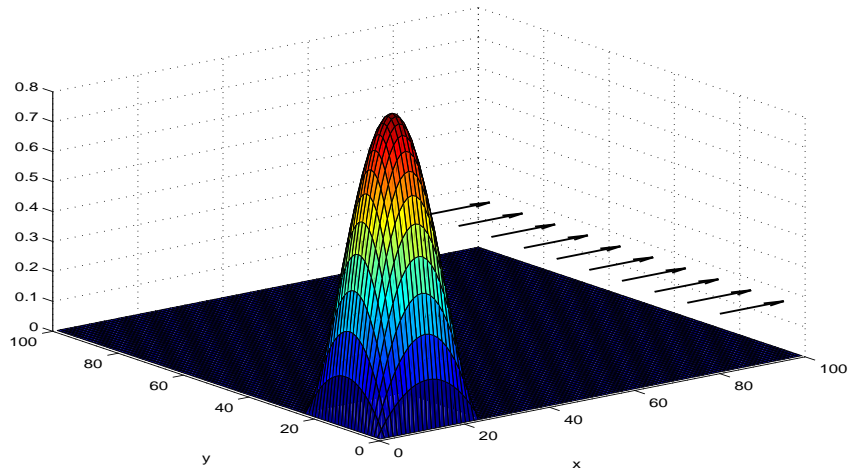


Lecture 2 - 2.1 Social Behaviors in Crowds

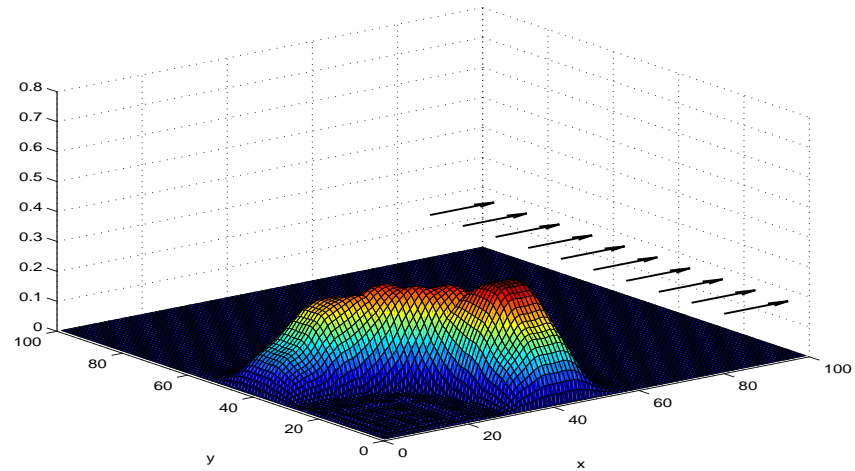
Case Study 2



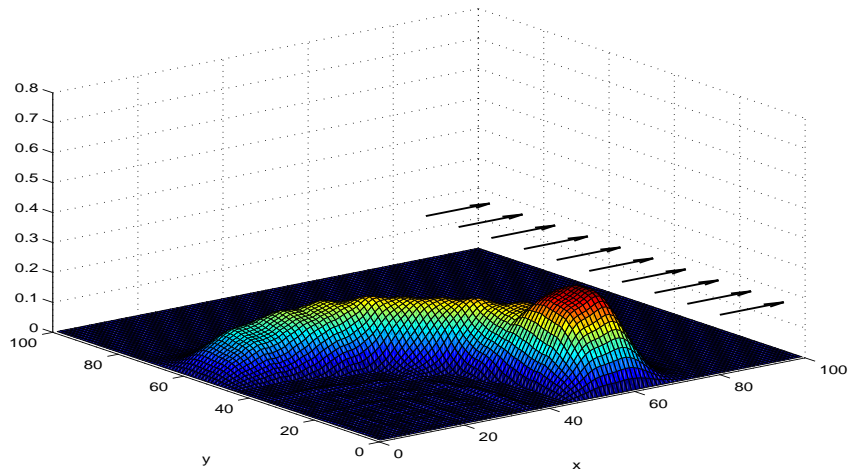
Lecture 2 - 2.1 Social Behaviors in Crowds



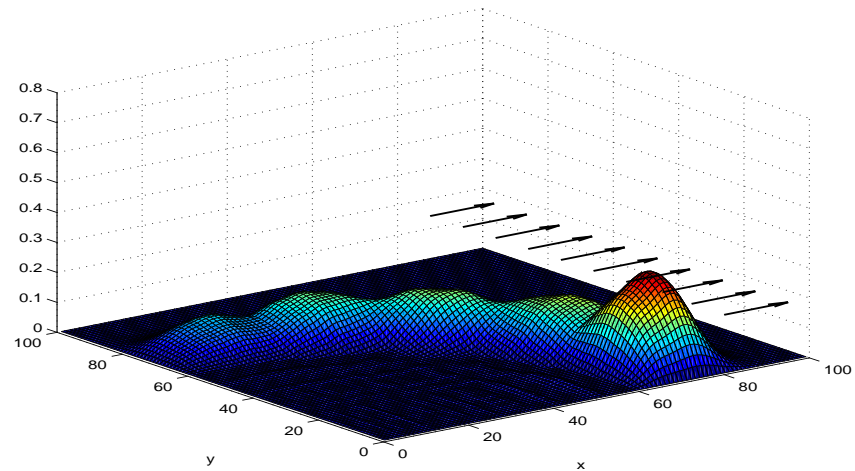
(c)



(d)



(e)

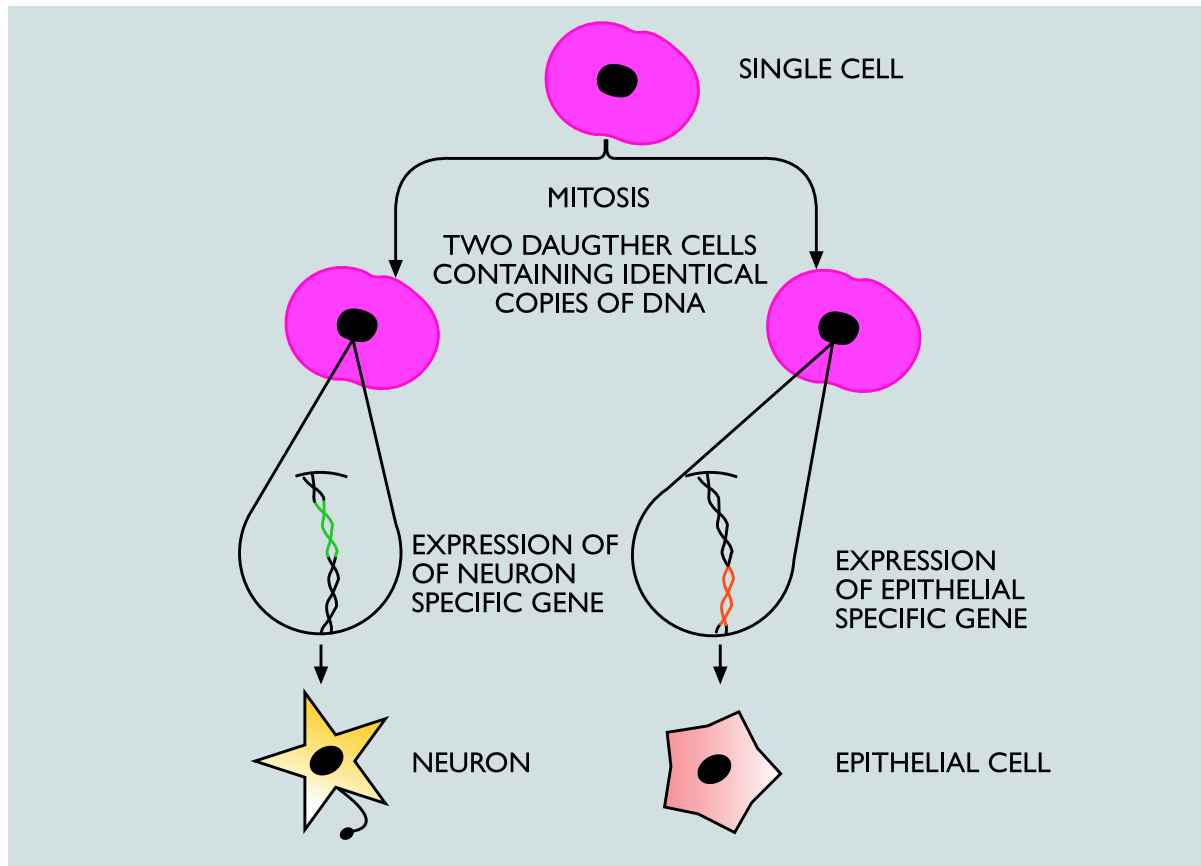


(f)

Lecture 2 - 2.2 System Biology and Immune Competition

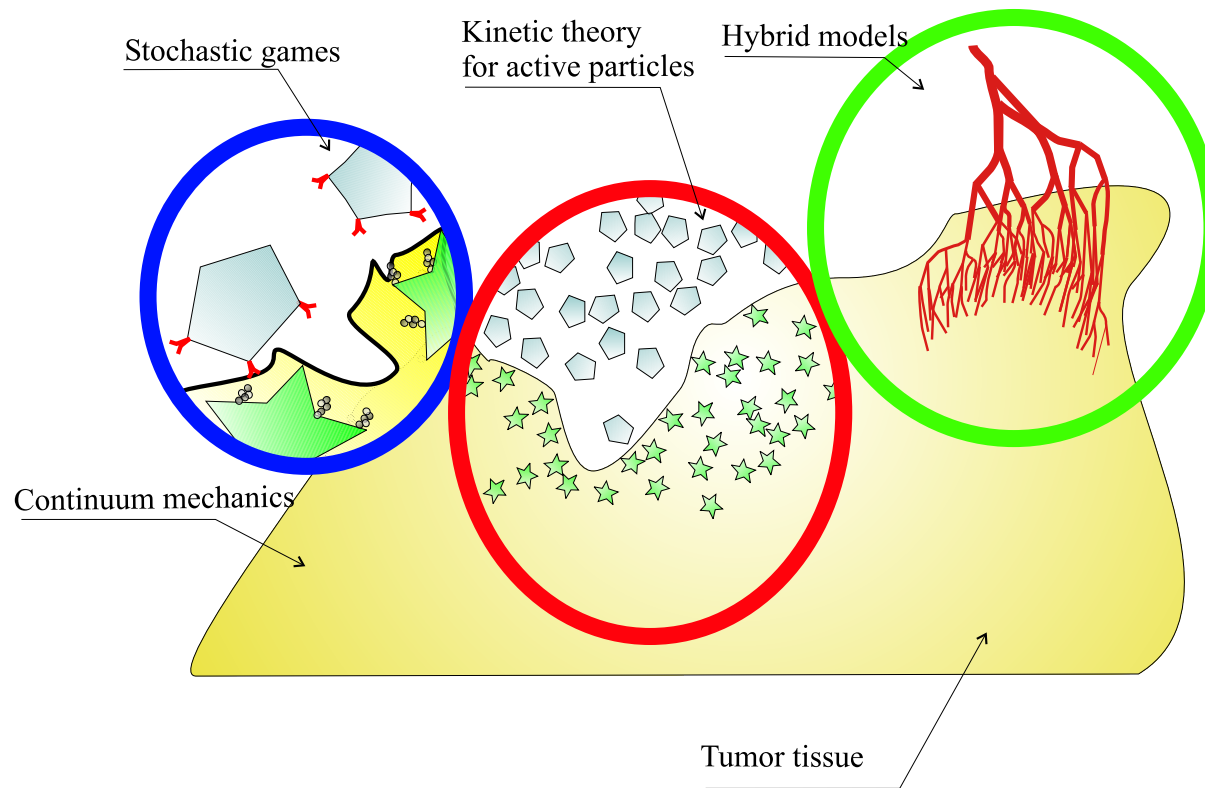
A Post-Darwinian Approach to Hallmarks of Cancer and Immune Cells

EVOLUTION OF CELLULAR PHENOTYPE



Lecture 2 - 2.2 System Biology and Immune Competition

MULTISCALE REPRESENTATION OF TUMOUR GROWTH: gene interactions (*stochastic games*), cells (*kinetic theory*), tissues (*continuum mechanics*), mixed (*hybrid models*).



N. Bellomo, A. Bellouquid, J. Nieto, and J. Soler, Modeling chemotaxis from L2-closure moments in kinetic theory of active particles *Discr. Cont. Dyn. Syst. - B*, 18 847–863, (2013).

Lecture 2 - 2.2 System Biology and Immune Competition

Phenomenological description

Multicellular systems involved in the immune competition are strongly related to the complexity features presented in Lecture 1. Therefore their modeling can be regarded as a challenging benchmark for the application of the mathematical tools developed in this paper. Moreover, the approach needs tackling the problem of reducing the overall complexity induced by the very large number of components involved in the competition.

D. Hanahan and R.A. Weinberg, Hallmarks of cancer: the next generation, *Cell* 144 (2011) 646–74.

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

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

Lecture 2 - 2.2 System Biology and Immune Competition

Immune competition

- **Mutations**, namely self-sufficiency in growth signals, insensitivity to anti-growth signals, evading apoptosis, limitless replicative potential, sustained angiogenesis, evading immune system attack, and tissue invasion and metastasis, incorporate some aspects of genetic mutation, gene expression, and evolutionary selection, **leads to malignant progression**.
- **This process can be contrasted by the immune defence** as 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*.
- **An important feature is the process of Darwinian selection**, which can potentially initiate in each birth process, where mutations bring new genetic variants into populations and natural selection then screens them. In some cases, such as the generation of daughters from mother cells, new cell phenotypes can originate from random mistakes during replication.

Lecture 2 - 2.2 System Biology 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. The subdivision into functional subsystems is reported in Table, where in particular:

↓	$i = 1$ 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 2 - 2.2 System Biology and Immune Competition

Mathematical structure

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

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: $I_u = \{0 = u_1, \dots, u_j, \dots, u_m = 1\}$. Therefore, the overall state of the system is described by the generalized 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 2 - 2.2 System Biology and Immune Competition

Interactions

- Conservative interactions, where 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} .
- Interactions can induce net proliferative events, which 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.
- Interactions can generate destructive events in the sense that 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 2 - 2.2 System Biology and Immune Competition

Interactions

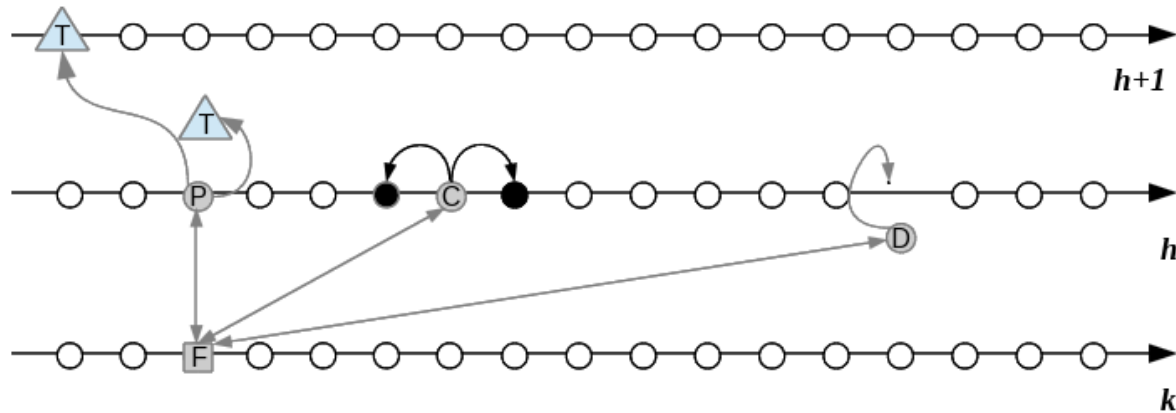


Figure 3: A h -candidate particle P (mother cell) by interaction with a k -field particle F proliferates giving a daughter cell T , belonging either to the same functional subsystem with same state (identical daughter), or to the following functional subsystem with the lowest activity value (mutated 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 2 - 2.2 System Biology 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 looses. 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 2 - 2.2 System Biology and Immune Competition

Simulations

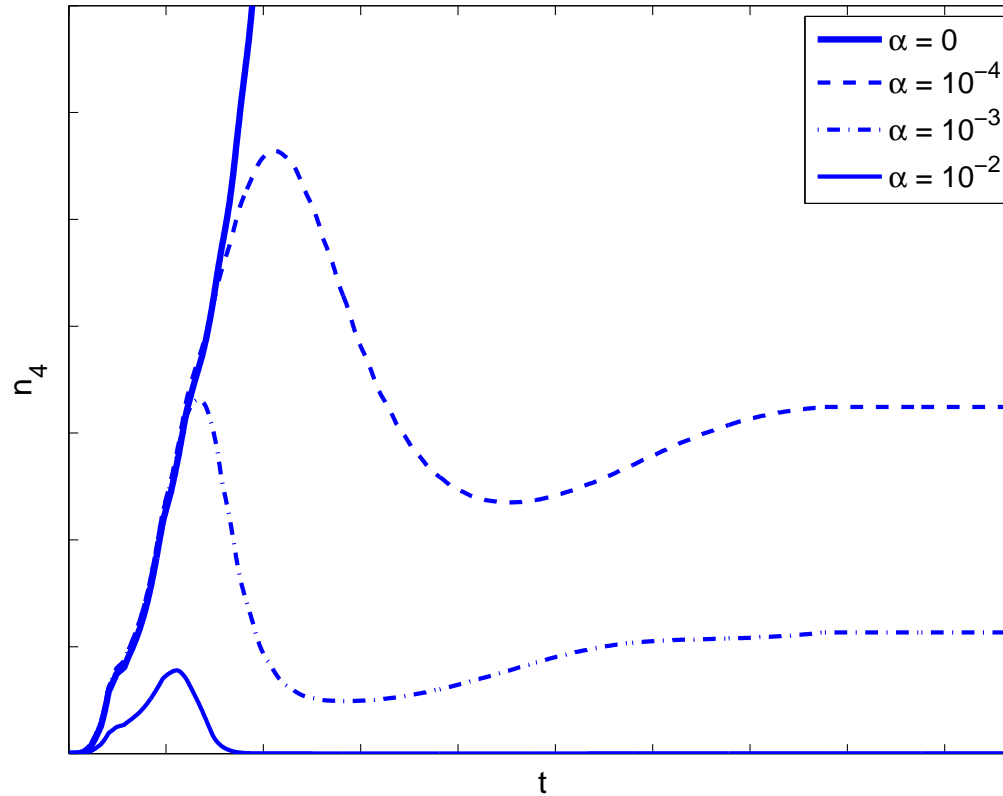


Figure 4: Time evolution of the density of the most aggressive tumor functional subsystem for different values of parameter α corresponding to the ratio between the rates of proliferation of the last immune and cancer hallmarks.

Plan of the Lectures

Lecture 1. From Some Reasonings on Complex Systems to a Modeling Strategy

Lecture 2. Two Applications:

2.1 Social Behaviors in Crowds

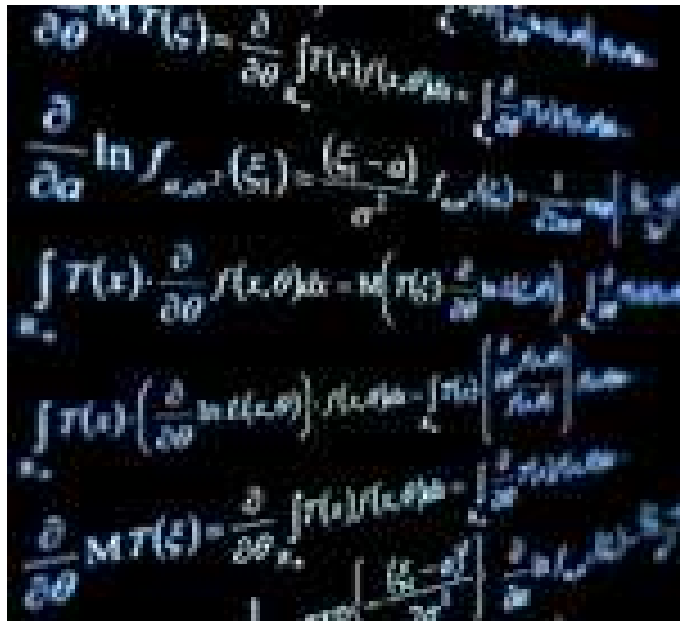
2.2 System Biology and Immune Competition

Lecture 3. Towards a Mathematical Theory of Living Systems (Looking for the Black swan)

Lecture 3 - Mathematical Theory of Living Systems

2. From Reasonings on Complex Systems to Mathematical Tools

- Looking for the black swan



Lecture 3 - Mathematical Theory of Living Systems

Selected Bibliography

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F.C. Santos, J.M. Pacheco, T. Lenaerts, Evolutionary dynamics of social dilemmas in structured heterogeneous populations, *Proc. Natl. Acad. Sci. USA*, 103(9) (2006), 3490–3494.

H. Gintis, *Game Theory Evolving: A Problem-Centered Introduction to Modeling Strategic Interaction*, Princeton University Press, Princeton, (2009).

M. Scheffer, J. Bascompte, W. A. Brock, V. Brovkin, S. R. Carpenter, V. Dakos, H. Held, E. H. van Nes, M. Rietkerk, and G. Sugihara, Early-warning signals for critical transitions, *Nature*, 461, 53–59, (2009).

N. Bellomo, D. Knopoff, and J. Soler, On the Difficult Interplay Between Life, “Complexity”, and Mathematical Sciences, *Math. Models Methods Appl. Sci.*, **23**, (2013).

N. Bellomo, M. Herrero, and A. Tosin, On the dynamics of social conflicts: looking for the Black Swan, *Kinetic and Related Models*, 6(3), (2013), 459–479.

Lecture 3 - Mathematical Theory of Living Systems

A question which is also a dilemma

Should mathematics attempt to reproduce experiments by equations whose parameters are identified on the basis of empirical data, or develop new structures, hopefully a new theory able to capture the complexity of biological phenomena and subsequently to base experiments on theoretical foundations?

This question witnesses the presence of a *dilemma*, which occasionally is the object of intellectual conflicts within the scientific community. However, we are inclined to assert the second perspective, since we firmly believe that it can also give a contribution to further substantial developments of mathematical sciences.

Should a conceivable mathematical theory show common features in all field of applications?

Although a theory should be linked to a specific class of systems, all theories should have common features.

Lecture 3 - Mathematical Theory of Living Systems

Strategy and Model Validation

- Models should be derived within mathematical structures suitable to include the aforesaid common features of living, hence complex, systems;
- The first step toward the validation of models consists in verifying that they describe quantitative results delivered in quasi steady states (corresponding to experiments) as an output of the dynamics at the micro-scale, without artificially inserting them into the model (for instance as a trend to an equilibrium);
- The the second step toward the validation of models consists in verifying that they describe, at least at a qualitative level, emerging collective behaviors observed in reality.

Lecture 3 - Mathematical Theory of Living Systems

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 rates* $\eta_{hk}[\mathbf{f}]$ and $\mu_{hk}[\mathbf{f}]$ 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 $\{\mathbf{v}, u\}$ 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 $\mu_{hk} \mathcal{P}_{hk}^i$, which denotes the proliferation rate into the functional subsystem i , due the encounter of particles belonging the functional subsystems h and k . Destructive events can occur only within the same functional subsystem with rate $\mu_{ik} \mathcal{D}_{ik}$.

Lecture 3 - Mathematical Theory of Living Systems

Balance within the space of microscopic states and Structures

Variation rate of the number of active particles

= *Inlet flux rate caused by conservative interactions*

+ *Inlet flux rate caused by proliferative interactions*

– *Outlet flux rate caused by destructive interactions*

– *Outlet flux rate caused by conservative interactions,*

where the inlet flux includes the dynamics of mutations.

This flow-chart 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} .

Lecture 3 - Mathematical Theory of Living Systems

Mathematical Structures

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

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

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

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

Lecture 3 - Mathematical Theory of Living Systems

Mathematical Structures

- **Interaction rates**, denoted by $\eta_{hk}[\mathbf{f}](\mathbf{w}_*, \mathbf{w}^*)$ and $\mu_{hk}[\mathbf{f}](\mathbf{w}_*, \mathbf{w}^*)$, which model the frequency of the interactions between a candidate h -particle with state \mathbf{w}_* and a field k -particle with state \mathbf{w}^* . Different rates η and μ are used corresponding to conservative and proliferative/destructive interactions, respectively.
- **Transition probability density** $\mathcal{C}_{hk}^i[\mathbf{f}](\mathbf{w}_* \rightarrow \mathbf{w}; \mathbf{w}^*)$, which denotes the probability density that a candidate h -particle ends up into the state of the test particle of the i -th functional subsystem after an interaction (with rate η_{hk}) with a field k -particle, while test i -particles interact with field particles and lose their state.
- **Proliferative term** $\mathcal{P}_{hk}^i[\mathbf{f}](\mathbf{w}_* \rightarrow \mathbf{w}; \mathbf{w}^*)$, which models the proliferative events for a candidate h -particle into the i -th functional subsystem after interaction (with rate μ_{hk}) with a field k -particle.
- **Destructive term** $\mathcal{D}_{ik}[\mathbf{f}](\mathbf{w}; \mathbf{w}^*)$, which models the rate of destruction for a candidate i -particle in its own functional subsystem after an interaction (with rate μ_{ik}) with a field k -particle.

Lecture 3 - Mathematical Theory of Living Systems

Mathematical Structures: Vanishing mechanical variables

The framework when space and velocity variables are not significant simplify as follows:

$$\begin{aligned}\partial_t f_i(t, u) &= [C_i[\mathbf{f}] + \mathcal{P}_i[\mathbf{f}] - \mathcal{L}_i[\mathbf{f}] - \mathcal{D}_i[\mathbf{f}]](t, u) \\ &= \sum_{h,k=1}^n \int_{D_u \times D_u} \eta_{hk}(u_*, u^*) \mathcal{C}_{hk}^i[\mathbf{f}](u_* \rightarrow u | u_*, u^*) f_h(t, u^*) f_k(t, u^*) du_* du^* \\ &+ \sum_{h,k=1}^n \int_{D_u} \int_{D_u} \mu_{hk}(u_*, u^*) \mathcal{P}_{hk}^i[\mathbf{f}](u_*, u^*) f_h(t, u^*) f_k(t, u^*) du_* du^* \\ &- f_i(t, u) \sum_{k=1}^n \int_{D_u} \eta_{ik}(u, u^*) f_k(t, u^*) du^* \\ &- f_i(t, u) \sum_{k=1}^n \int_{D_u} \mu_{ik}(u, u^*) \mathcal{D}_{ik}[\mathbf{f}] f_k(t, u^*) du^*,\end{aligned}$$

Lecture 3 - Mathematical Theory of Living Systems

Sources of nonlinearity

- **Sensitivity and space interaction domains:** A candidate (or test) particle interacts with a number of field particles by means of a communication ability that is effective only within a certain *domain of influence* of the space variable $\Omega_I[\mathbf{f}]$, which depends on the maximal density of active particles which can be captured in the communication. This domain is effective only if it is included in the *sensitivity domain* $\Omega_S(\mathbf{x})$, within which active particles have the potential ability to feel the presence of another particles.
- **Partial sensitivity:** If $\Omega_I \subseteq \Omega_S$ the active particle receives sufficient information to fully develop the standard strategy without restrictions. On the other hand, when $\Omega_S \subset \Omega_I$, interactions are not sufficient to fully develop their strategy. We adopt the notation $\Omega[\mathbf{f}, \mathbf{x}] = \Omega_I[\mathbf{f}] \cap \Omega_S(\mathbf{x})$ to denote the effective interaction domain. In some special case this domain might be equal to zero so that particles do not modify their trajectory.

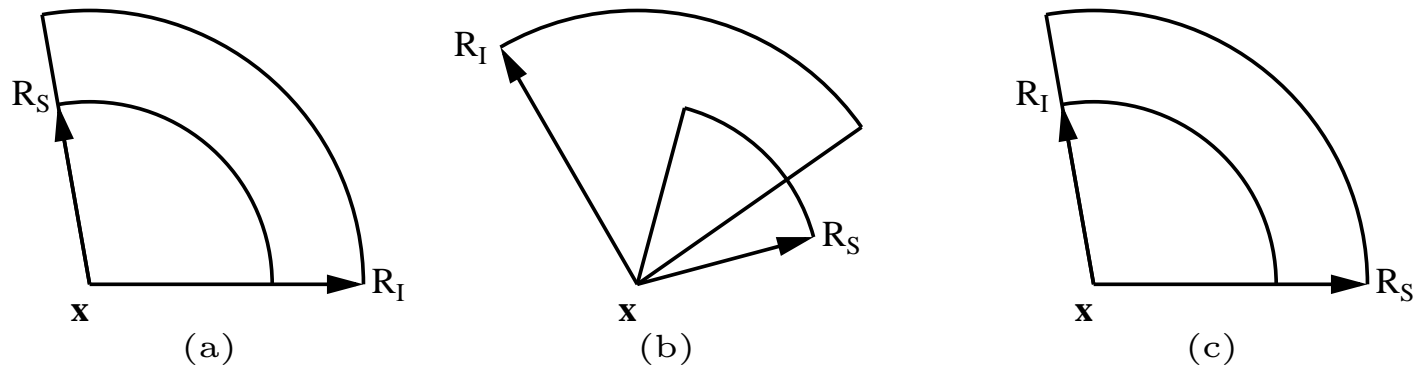
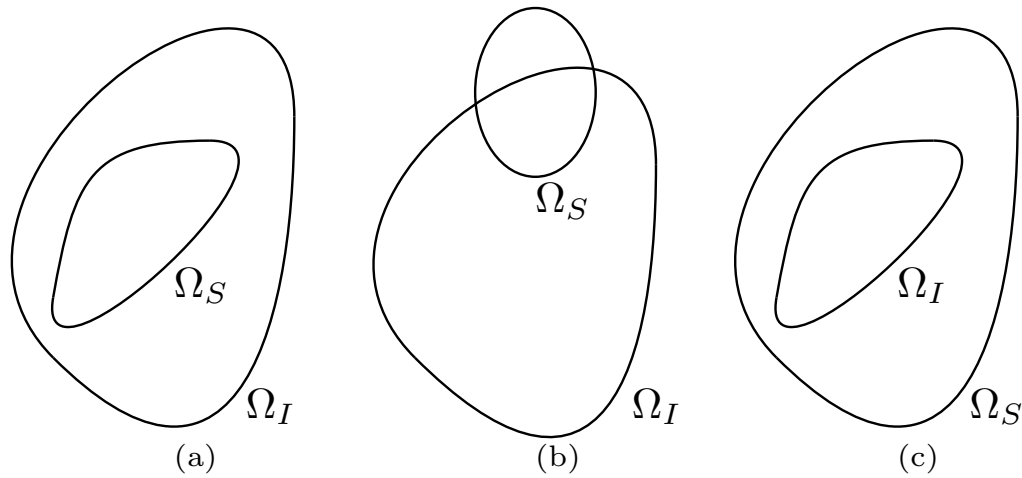
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Sources of nonlinearity with influence on the encounter rate

- **Micro-state distance:** $|\mathbf{w}_* - \mathbf{w}^*| = |(\mathbf{x}_*, \mathbf{v}_*, u_*) - (\mathbf{x}^*, \mathbf{v}^*, u^*)|$ between the micro-states by a suitable metric. to be considered for each specific case.
- **Individual-mean state distance:**, which refers the state \mathbf{w}_* to the mean value of \mathbf{w}^* in the domain of interactions of the field particles according to a suitable metric. Such a distance can be formally denoted as follows: $|\mathbf{w}_* - \mathbf{E}_\Omega(\mathbf{w}^*)|$.
- **Hierarchic distance:** which occurs when two active particles belong to different functional subsystems. Then the distance $|k - h|$ can be defined if a conceivable numbering criterion is applied in selecting the first subsystem by a certain selection rule (for instance, in the animal world, the “dominant”) and in numbering the others by increasing numbers depending on the decreasing rate.
- **Affinity distance:** According to the general idea that two systems with close distributions are *affine*. In this case the distance is $\|f_h - f_k\|_{L^p(\Omega[\mathbf{f}])}$.

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Sources of nonlinearity



Lecture 3 - Mathematical Theory of Living Systems

Looking for the Black Swan in Social Dynamics

- 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..
- 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 models should also focus, in particular, on the prediction of the so called *Black Swan*.** The latter is defined to be a rare event, showing up as an irrational collective trend generated by possibly rational individual behaviors.

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Looking for the Black Swan in Social Dynamics

G. Ajmone Marsan, N. Bellomo, and A. Tosin, **Complex Systems and Society - Modeling and Simulations**, *Springer Briefs*, Springer, New York, (2013).

- Living → active entities
- Behavioral strategies, bounded rationality → randomness of human behaviors
- Heterogeneous distribution of strategies → stochastic games
- Behavioral strategies can change in time
- Self-organized collective behavior can emerge spontaneously: In particular the so-called Black Swan.

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Looking for the Black Swan in Social Dynamics Complexity Features of Social Systems

- Social classes: (poor) $u_1 = -1, \dots, u_i, \dots, u_n = 1$ (wealthy)
- Political opinion: (dissensus) $v_1 = -1, \dots, v_r, \dots, v_m = 1$ (consensus)
- Distribution function: $f_i^r(t) = \#$ people in u_i with opinion v_r at time t

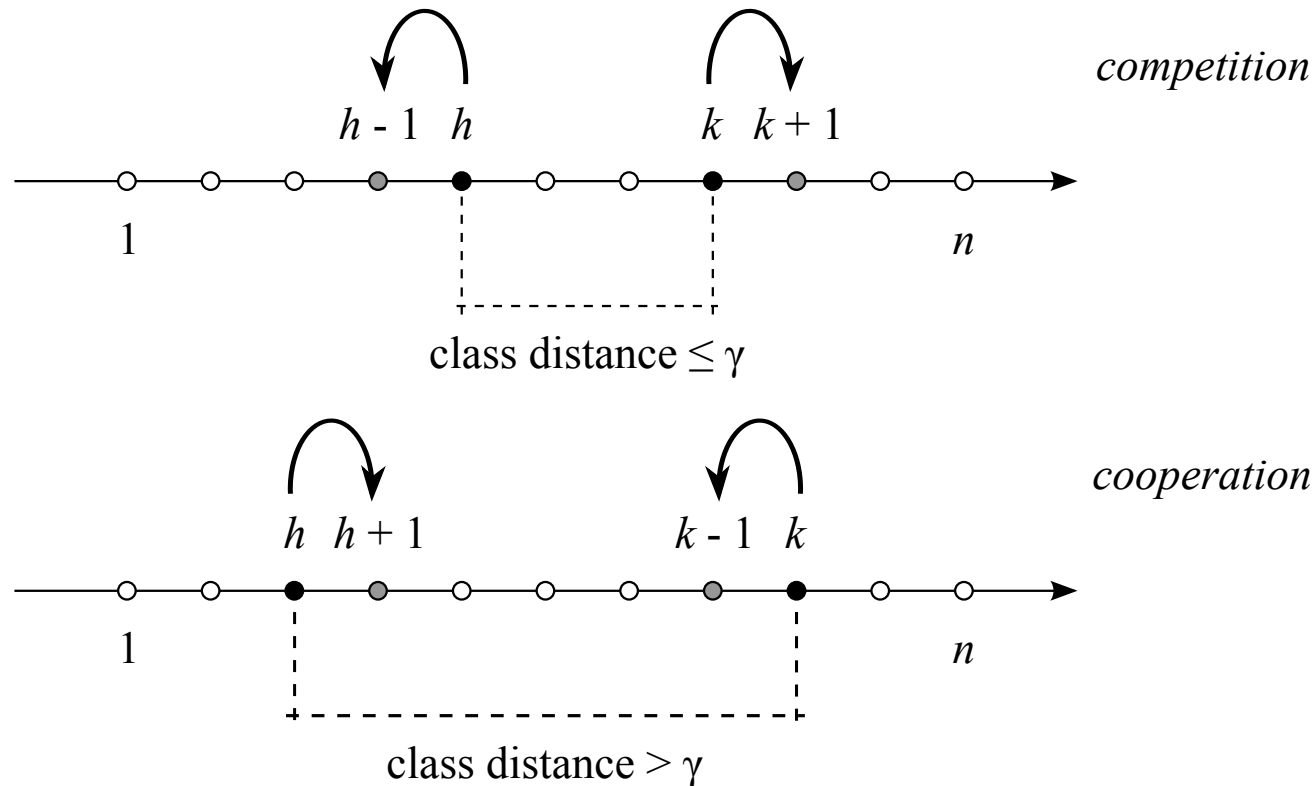
$$\frac{df_i^r}{dt} = \underbrace{\sum_{p,q=1}^m \sum_{h,k=1}^n \eta_{hk}^{pq} A_{hk}^{pq}(i,r) f_h^p f_k^q}_{\text{Gain}} - f_i^r \underbrace{\sum_{q=1}^m \sum_{k=1}^n \eta_{ik}^{rq} f_k^q}_{\text{Loss}}$$

$$A_{hk}^{pq}(i,r) := \mathbb{P}((u_h, v_p) \rightarrow (u_i, v_r) | (u_k, v_q))$$

$$\sum_{r=1}^m \sum_{i=1}^n A_{hk}^{pq}(i,r) = 1, \quad \forall h, k = 1, \dots, n, \quad \forall p, q = 1, \dots, m.$$

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Looking for the black swan in Social Dynamics



A critical distance triggers either cooperation or competition among the classes. If the distance is lower than the critical one then a competition takes place. Conversely, if the actual distance is greater than the critical one then the social organization forces cooperation.

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Looking for the black swan in Social Dynamics

- *Interaction rate.* Two different rates of interaction are considered, corresponding to competitive and cooperative interactions, respectively.
- *Strategy leading to the transition probabilities.* When interacting with other particles, each active particle plays a game with stochastic output. If the difference of wealth class between the interacting particles is lower than a critical distance $\gamma[\mathbf{f}]$ (where, here and henceforth, square brackets indicate a functional dependence on the probability distribution \mathbf{f}) then the particles compete in such a way that those with higher wealth increase their state against those with lower wealth. Conversely, if the difference of wealth class is higher than $\gamma[\mathbf{f}]$ then the opposite occurs. The critical distance evolves in time according to the global wealth distribution over wealthy and poor particles.
- The *critical distance* $\gamma[\mathbf{f}]$ is here assumed to depend on the instantaneous distribution of the active particles over the wealth classes, such that the time evolution of $\gamma[\mathbf{f}]$ such that it grows with the number of poor active particles, thus causing larger and larger gaps of social competition.

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Looking for the black swan in Social Dynamics

$$S[\mathbf{f}] := N^-[\mathbf{f}] - N^+[\mathbf{f}] = \sum_{i=1}^{\frac{n-1}{2}} f_i(t) - \sum_{i=\frac{n+3}{2}}^n f_i(t).$$

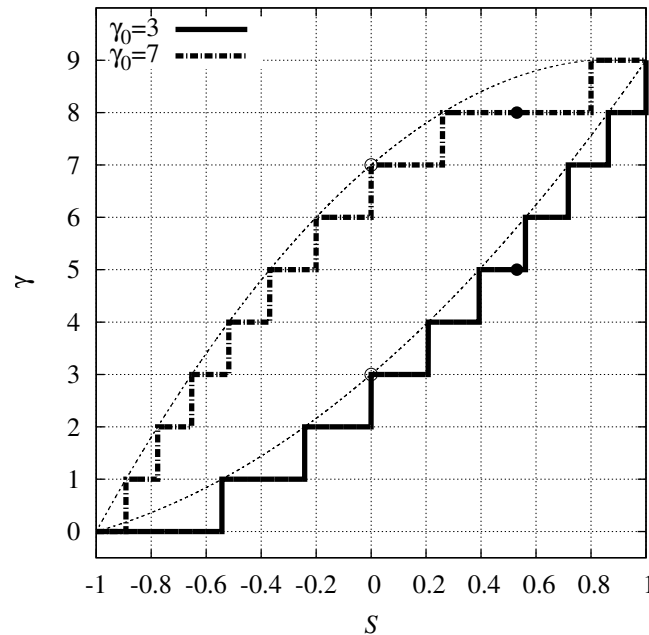
- $S[\mathbf{f}] = S_0 \Rightarrow \gamma[\mathbf{f}] = \gamma_0$, where S_0, γ_0 are a reference social gap and the corresponding reference critical distance, respectively;
- $S[\mathbf{f}] = 1 \Rightarrow \gamma[\mathbf{f}] = n$: when the population is composed by poor particles only ($N^- = 1, N^+ = 0$) the socio-economic dynamics are of full competition;
- $S[\mathbf{f}] = -1 \Rightarrow \gamma[\mathbf{f}] = 0$: when the population is composed by wealthy particles only ($N^- = 0, N^+ = 1$) the socio-economic dynamics are of full cooperation.

$$\gamma[\mathbf{f}] = \frac{2\gamma_0(S[\mathbf{f}]^2 - 1) - n(S_0 + 1)(S[\mathbf{f}]^2 - S_0)}{2(S_0^2 - 1)} + \frac{n}{2}S[\mathbf{f}],$$

where \cdot denotes integer part (floor).

3 - Modeling Social Conflicts and Political Competition

Dynamics of the threshold



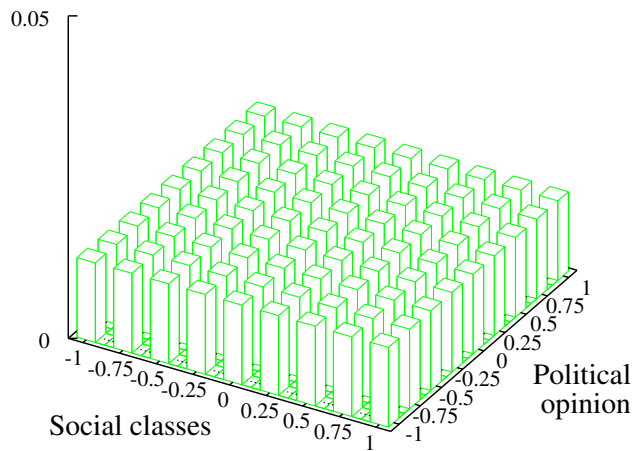
Piff, P.K., Stancato, D.M., Ceote, S., Mendoza-Denton, R., Keltner, D., Higher social class predicts increased unethical behavior, *Proceedings of the National Academy of Sciences*, 109(11), 40864091 (2012).

OECD, *Divided We Stand: Why Inequality Keeps Rising?* OECD Publishing (2011) 129.

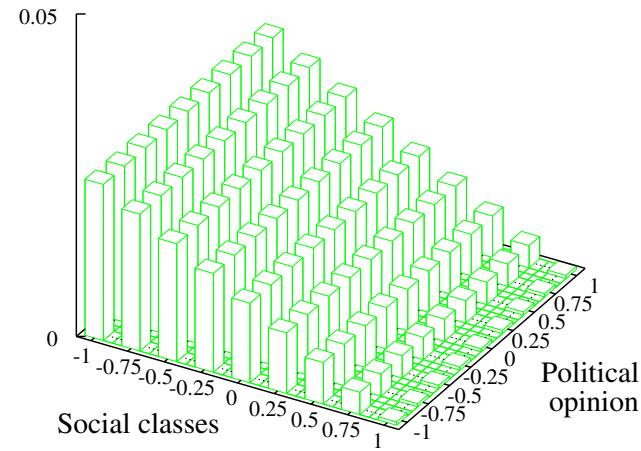
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Looking for the black swan in Social Dynamics Case Studies

- Initial conditions



Society “neutral” on average
Mean wealth: 0

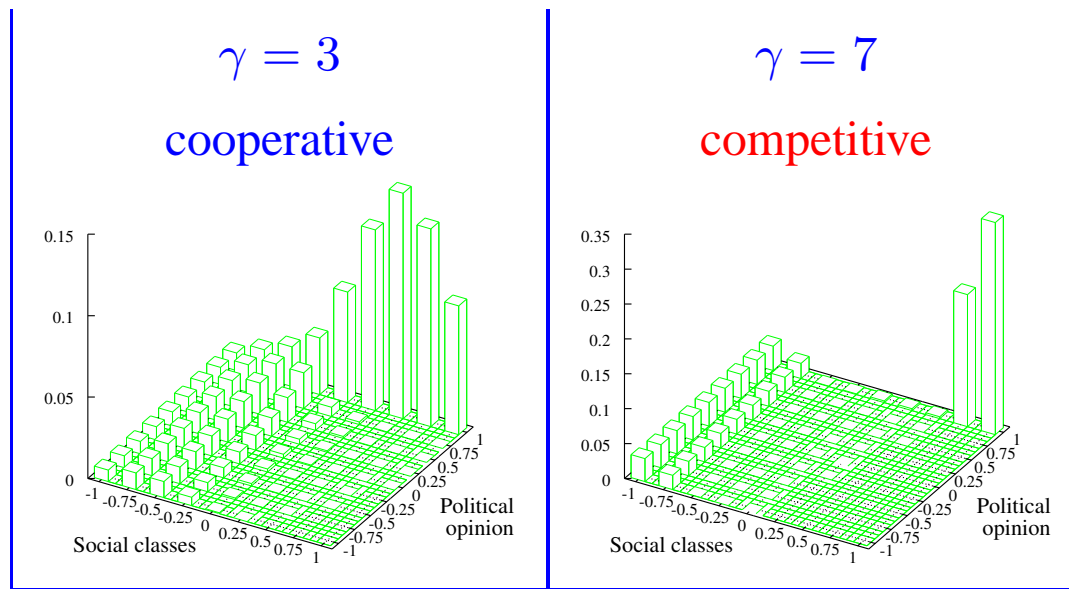


Society poor on average
Mean wealth: -0.4

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Looking for the black swan in Social Dynamics

- Society which is “economically neutral” on average



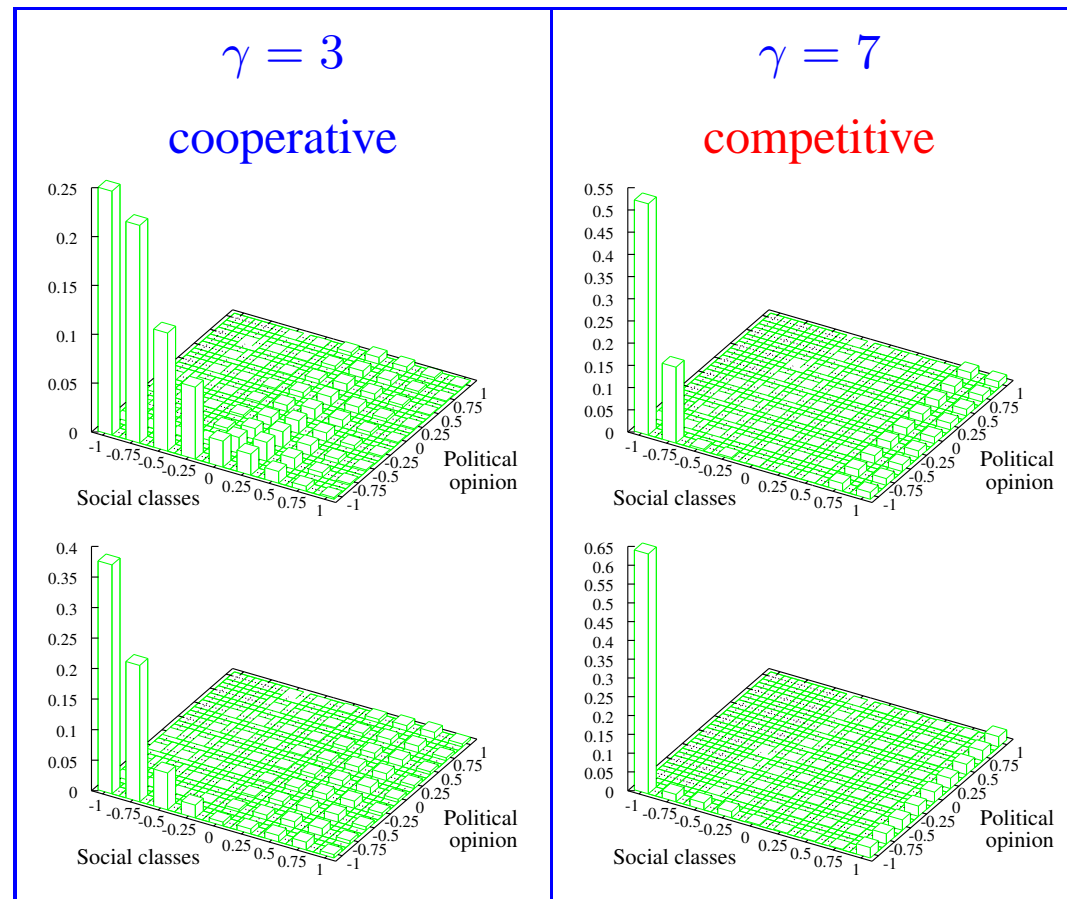
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Looking for the black swan in Social Dynamics

- Society which is poor on average

constant γ

variable γ



Lecture 3 - Mathematical Theory of Living Systems

Looking for the black swan in Social Dynamics

Simulations $n = 9$ and $\mu = 0.3$

This Figure refers to the case $U_0 = 0$, and shows that:

- In an economically neutral society with uniform wealth distribution not only do wealthy classes stick at an earnest support to the Government policy, but also poor ones do not completely distrust them, especially in a context of prevalent cooperation among the classes ($\gamma_0 = 3$).
- Therefore, this example does not suggest the development of significant polarization in that society, although a greater polarization is observed for higher values of γ .

Lecture 3 - Mathematical Theory of Living Systems

Looking for the black swan in Social Dynamics

Early Signals of a Black Swan: Let us assume that a specific model has a trend to an asymptotic configuration described by stationary distributions $\{\bar{f}_i^r\}_{i=1, \dots, n}^{r=1, \dots, m}$:

$$\lim_{t \rightarrow +\infty} \|\bar{f}^r - f^r(t)\| = 0, \quad \forall r = 1, \dots, m,$$

where $\|\cdot\|$ is a suitable norm in n over the activity $u \in I_u$. In addition, let us assume that the modeled system is expected to exhibit a stationary trend described by some phenomenologically guessed distributions $\{\tilde{f}_i^r\}_{i=1, \dots, n}^{r=1, \dots, m}$.

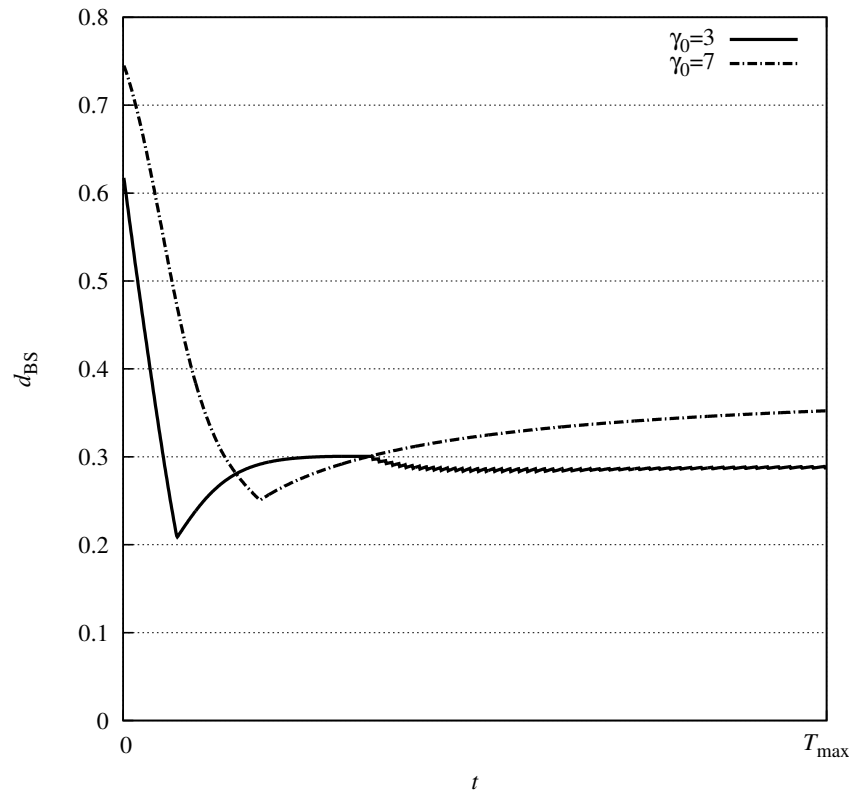
Accordingly, we define the following time-evolving distance d_{BS} (the subscript “BS” standing for Black Swan):

$$d_{\text{BS}}(t) := \max_{r=1, \dots, m} \|\tilde{f}^r - f^r(t)\|,$$

which, however, will generally not approach zero as time goes by for the heuristic asymptotic distribution does not translate the actual trend of the system. This function can be possibly regarded as one of the *early-warning signals* for the emergence of critical transitions to rare events, because it may highlight the onset of strong deviations from expectations.

3 - Modeling Social Conflicts and Political Competition

Early Signals of the Black Swan



The mapping $t \mapsto d_{BS}(t)$ computed in the case studies with variable γ , taking as phenomenological guess the corresponding asymptotic distributions obtained with constant γ .

End of the Lectures - Thanks

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