

Modelos estocásticos en Física, Biología y Ciencias Sociales

LIBRO DE ABSTRACTS

MINICURSOS

Matemáticas de la evolución

Prof. José A. Cuesta Ruiz

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Resumen: Con frecuencia se oye la crítica de que la teoría evolutiva es tautológica, porque postula la supervivencia de los más aptos, y los más aptos son aquellos que sobreviven. Pese a esta burda simplificación de lo que es la teoría evolutiva, lo cierto es que admite formulaciones matemáticas que permiten hacer predicciones cuantitativas. Teniendo en cuenta ingredientes básicos como la genética, el azar y la aptitud (entendida como número de descendientes que un individuo deja en la siguiente generación), se construyen diversos procesos evolutivos, en esencia estocásticos, con los cuales se puede estudiar la influencia de diversos factores en la evolución de las especies. Una de las herramientas básicas, introducida en la biología en los años 70, es la que se ha dado en denominar teoría de juegos evolutiva. Gracias a esta formulación la misma teoría da cuenta de la evolución de comportamientos y fenómenos sociales, como formación de opiniones, competición lingüística, etc. En esta serie de charlas intentaré hacer una panorámica de las ecuaciones y la matemática que permite describir los procesos evolutivos, tanto a nivel biológico como social.

Bibliografía:

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[C2] M. A. Nowak, "Evolutionary Dynamics: Exploring the Equations of Life" (Belknap Press, 2006).

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Introducción a la teoría matemática del movimiento browniano, la fórmula de Feynman y Kac, con aplicaciones.

Prof. F. Alberto Grünbaum

Departamento de Matemáticas, Universidad de California, Berkeley

Resumen: Mi intención es presentar -sin demasiados detalles técnicos- los rudimentos de la medida de Wiener definida en el espacio de funciones continuas y discutir algunas propiedades del movimiento browniano que da origen a esta construcción. La medida de Wiener permite resolver la ecuación del calor mediante integración en un espacio de funciones. En el caso más interesante en que uno agrega un potencial $V(x)$ en la ecuación del calor la correspondiente solución está dada por la fórmula de Feynman y Kac. Como aplicación discutiremos resultados vinculados a juegos de azar.

Bibliografía:

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[A2] K.Ito and H.P. McKean, Diffusion processes and their sample paths, Classics in Mathematics, Springer-Verlag, 1996.

[A3] M. Kac, On some connections between probability theory and differential and integral equations Proc 2nd Berkeley Symp. on Math. Stat. & Prob. (1951) 189-215.

Juegos de azar y motores brownianos.

Prof. Juan M.R. Parrondo

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Resumen: Los sistemas aleatorios dan lugar a fenómenos sorprendentes e inesperados. Uno de ellos es la llamada Paradoja de Parrondo, en la que dos juegos de azar perdedores dan lugar a uno ganador cuando se alternan. La paradoja está inspirada en un sistema físico de interés en Biología: los motores brownianos, y ha motivado toda una serie de estudios sobre efectos no triviales en la alternancia de dinámicas aleatorias y sus posibles aplicaciones en Biología, Economía o Ecología. Utilizando herramientas básicas, como la teoría de cadenas de Markov, haremos una revisión de la paradoja y sus variaciones, así como de sus distintas aplicaciones.

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CONFERENCIAS PLENARIAS

The effects of thermal noise on transport in soliton ratchet systems.

Prof. Franz G. Mertens

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Abstract: Ratchet or rectification phenomena appear in various fields ranging from nanodevices (e.g., Josephson junctions) to biophysics (e.g., molecular motors). In the simplest model a pointlike particle can perform a unidirectional motion on the average, although the driving force has zero average in time, if certain conditions related to the breaking of symmetries hold. Such particle ratchets have been generalized to spatially extended systems, in which solitons play a similar role as the above point particles.

We study the influence of thermal noise on soliton transport in three types of nonlinear Klein-Gordon ratchet systems:

- 1.) homogeneous systems in which a temporal symmetry is broken by using a biharmonic driving force,
- 2.) inhomogeneous systems in which the spatial symmetry is broken by introducing a potential with strongly localized inhomogeneities,
- 3.) systems with additive inhomogeneities (in contrast to the previous case in which the inhomogeneities were multiplicative).

We add Gaussian white noise to a nonlinear Klein-Gordon equation and solve numerically the resulting stochastic PDE. This yields the average soliton velocity as a function of the model parameters. The results are compared with a Collective-CoordinateTheory which yields a set of stochastic ODEs, which are solved numerically.

Thermal noise has the following main effects:

- a) the ratchet effect is robust for not too high temperatures. In fact, the average soliton velocity may even be enhanced in certain cases,
- b) the so-called "windows" (defined as regions in which there is a non-zero ratchet effect), which appear in the deterministic models, are broadened and smeared out due to the noise,
- c) in type 2 systems, for a very narrow frequency range a new window appears in a regime where no window existed in the deterministic case. This effect has some similarity with Stochastic Resonance.

Bibliografía:

- [1] A. Sanchez, L. Morales-Molina, F.G. Mertens, N.R. Quintero, J. Buceta and K. Lindenberg, *Fluct. and Noise Lett.* 4, L571 (2004)
- [2] L. Morales-Molina, F.G. Mertens, and A. Sanchez, *Phys. Rev. E* 72, 016612 (2005)
- [3] V. Stehr, P. Mueller, F.G. Mertens and A.R. Bishop, submitted (2008)

Stochastic effects in infection dynamics.

Prof. Ana Nunes

Centro de Física Teórica y Computacional, Univ. de Lisboa, Portugal.

Abstract: During the last decade, more sophisticated approaches building on the traditional SIR and SEIR models have brought considerable advances in understanding and selecting some of the fundamental ingredients of the complex dynamics of infectious diseases [1]. This body of work belongs to an essentially deterministic framework, where demographic stochasticity plays a secondary role, that of sustaining small amplitude fluctuations around the deterministic system's equilibrium that follow the natural frequency given by the local linear approximation [2].

In population biology, stochasticity comes from the discrete interactions and the disordered interaction networks, and fluctuations and finite size effects in general are much more important than in typical physical systems. Indeed, recent results show that for realistic population sizes, the behaviour of predator-prey and of epidemic or endemic infections may be driven by the combined effect of fluctuations and correlations. In [3], a general mechanism of resonant amplification of demographic stochasticity was proposed to describe the cycling behaviour of prey-predator systems. This resonant mechanism is generic for a class of stochastic systems that includes the majority of the classical models of diseases that confer either lifelong or temporary total immunity, and it was shown in [4] that it plays a major role in describing the patterns of recurrent epidemics of childhood infectious diseases. In [5], that approach was extended by adding an ingredient which is missing in standard epidemic models, the 'mixing network' through which infection may propagate. It was shown that correlations have a major effect in the enhancement of the amplitude and the coherence of the resonant stochastic fluctuations, providing ordered patterns of recurrent epidemics, whose period may differ significantly from that of the small oscillations around the deterministic equilibrium.

We shall review the main results of [1-5], and then explore analytic models where the assumptions of random mixing of the population and/or of constant recovery rate during the infectious period are relaxed, and see how this implies important corrections to the amplitude and dominant frequency of the stochastic fluctuations. The finding that in finite, discrete populations internal noise together with correlations produces sustained incidence oscillations of significant amplitude all over the parameter region that includes childhood

infectious diseases is of importance for the long-standing controversy in epidemiology and ecology as to the driving mechanisms of the pervasive noisy oscillations observed in these systems.

References:

- [1] D. J. D. Earn, P. Rohani, B. M. Bolker and B. T. Grenfell, A Simple Model for Complex Dynamical Transitions in Epidemics, *Science* 287, 667-670 (2000)
- [2] C. T. Bauch and D. J. D. Earn, Transients and attractors in epidemics, *Proc. R. Soc. Lond. B* 270, 1573-1578 (2003)
- [3] A.J. McKane, T.J. Newman, "Predator-Prey Cycles from Resonant Amplification of Demographic Stochasticity", *Physical Review Letters*, 94, 218102 (2005);
- [4] D. Alonso, A. J. McKane, M. Pascual, "Stochastic amplification in epidemics", *J R Soc Interface* 4, 575-82 (2007).
- [5] M. Simões, M. Telo da Gama and A. Nunes, "Stochastic fluctuations in epidemics on networks", *J R Soc Interface* 5, 555-66 (2008).

Dynamic realization games in newsvendor inventory centralization

Prof. Justo Puerto

Departamento de Estadística e Investigación Operativa, Universidad de Sevilla

Abstract: Consider a set N of n (>1) stores with single-item and single-period nondeterministic demands like in a classic newsvendor setting with holding and penalty costs only. Assume a risk-pooling single-warehouse centralized inventory ordering option. Allocation of costs in the centralized inventory ordering corresponds to modelling it as a cooperative cost game whose players are the stores. It has been shown that when holding and penalty costs are identical for all subsets of stores, the game based on optimal expected costs has a non empty core (Hartman et al. 2000, *Games Econ Behav* 31:26–49; Muller et al. 2002, *Games Econ Behav* 38:118–126). In this talk we examine a related inventory centralization game based on demand realizations that has, in general, an empty core even with identical penalty and holding costs (Hartman and Dror 2005, *IIE Trans Scheduling Logistics* 37:93–107). We propose a repeated cost allocation scheme for dynamic realization games based on allocation processes introduced by Lehrer (2002a, *Int J Game Theor* 31:341–351). We prove that the cost subsequences of the dynamic realization game process, based on Lehrer's rules, converge almost surely to either a least square value or the core of the expected game. We extend the above results to more general dynamic cost games and relax the independence hypothesis of the sequence of players' demands at different stages.

The Feynman-Kac formula and its application in financial mathematics.

Prof. Jorge Zubelli

Instituto de Matemáticas Puras y Aplicadas, Rio de Janeiro, Brasil.

Abstract: In recent years there has been a substantial amount of theoretical work motivated by applications of analysis and probability to financial mathematics. Part of this activity is due to the importance of Black-Scholes type models and its connection to partial differential equations through Feynman-Kac formula. In this talk we will try to explain this connection without assuming previous background in mathematical finance. We shall also explore some recent applications of the theory to the problem of computing the sensitivity of the financial models to the different parameters and some generalizations.

CHARLAS CORTAS

Título: *Modelización de la evolución viral mediante la teoría de cuasiespecies: crecimiento y extinción.*

Prof. Jacobo Aguirre Araujo
Centro de Astrobiología (CSIC-INTA)

Abstract: En el contexto de la teoría de cuasiespecies [1], se presentó en 2003 un modelo discreto de campo medio para la evolución de poblaciones de replicadores con alta tasa de mutación [2]. Dicho modelo reproduce satisfactoriamente el crecimiento exponencial de las poblaciones y su tendencia hacia una distribución de equilibrio para su heterogeneidad fenotípica, ambos fenómenos observados experimentalmente en virus de RNA. Más adelante, extendimos el modelo al estudio de la expansión de una población de cuasiespecies en 2 dimensiones [3]. A pesar de la complejidad del crecimiento, ahora lineal y circunscrito a la frontera que separa a la población del medio circundante, mostramos que es posible caracterizar analíticamente la dinámica del sistema mediante una matriz cuyos elementos son las probabilidades de transición entre los diferentes estados fenotípicos. A diferencia, sin embargo, del caso de campo medio previamente estudiado, la difusión y los fenómenos locales de correlación resultan ser de importancia, y uno de los objetivos de este trabajo es el estudio de su influencia sobre la evolución del crecimiento viral.

En esta presentación explicaremos brevemente los modelos citados de crecimiento de virus en líquidos y superficies, así como un trabajo aún en desarrollo: su aplicación al estudio de la extinción de virus por mutagénesis letal. Este fenómeno consiste en aumentar la tasa de mutación de un virus (a través de mutágenos) con la finalidad de disminuir su *fitness* y, si es posible, impedir su replicación. El trabajo consta de dos partes: un análisis teórico del problema desde la perspectiva de la percolación dirigida, y una comprobación experimental de los resultados centrada en el uso en el laboratorio de placas de lisis producidas por virus en agar semisólido.

Bibliografía:

- [1] M. Eigen, Selforganization of matter and the evolution of biological macromolecules, *Naturwissenschaften* 58, 465-523 (1971).
- [2] S. C. Manrubia, E. Lázaro, J. Pérez-Mercader, C. Escarmís and E. Domingo, Fitness distributions in exponentially growing asexual populations, *Phys. Rev. Lett.* 90, 188102 (2003).
- [3] J. Aguirre and S. C. Manrubia, Effects of spatial competition on the diversity of quasispecies, *Phys. Rev. Lett.* 100, 038106 (2008).

El ensamblado de ecosistemas como una cadena de Markov.

Prof. José Ángel Capitán Gómez
Departamento de Matemáticas, Universidad Carlos III de Madrid

Abstract: Proponemos un modelo teórico sencillo de ecosistema del cual podemos caracterizar todos las posibles invasiones entre comunidades viables. Esto nos permitirá trasladar el proceso de "*ensamblado*" de comunidades a una cadena de Markov, y por tanto calcular de forma exacta todas las propiedades del proceso de generación de las comunidades. Los resultados más relevantes del modelo son: los ecosistemas se hacen cada vez más resistentes a la invasión, su biodiversidad aumenta, se obtienen estados absorbentes complejos que, además, resultan ser independientes de la historia del proceso de ensamblado.

Digital fabrication or: How I learned to stop worrying and love Lego bricks?

Prof. Luis Lafuente

Center for Bits and Atoms, Massachusetts Institute of Technology

Abstract: In the late 30s Shannon proved that it is possible to communicate perfectly (error-free) even through a noisy channel. Later, Von Neumann, Winograd and Cowan proved that reliable computation was also possible in the presence of noise. These works give birth to modern digital era, where digital coding can allow an imperfect system to send a message perfectly and to calculate perfect answers. In this talk, using digital communication and computation as analogies, I'll introduce digital fabrication (the revolution to come in manufacturing technology) and I'll show how imperfect machines can make complex perfect parts (an example of this taken from Biology is the ribosome making proteins). Finally, I will point out the necessity to develop a rigorous mathematical theory for digital fabrication.

Título: *A model of T population dynamics based on cross regulation and stochasticity*

Prof. Nieves Vélez de Mendizábal

Neuroimmunology Laboratory, Center for Applied Medical Research, University of Navarra

Abstract: The relapsing dynamics is a hallmark of autoimmune diseases such as multiple sclerosis. Although current understanding of the cells and molecules involved in the pathogenesis of autoimmune diseases is significant, how their activity generates this prototypical dynamics is not understood yet. Previous models of cross-regulation between effector and regulatory T-cells have shown bi-stable regimes with two steady stable points [1;2]. While the first focus refer to a situation where regulatory population overcomes effector population (healthy state), the second focus refer to the presence of mostly effector T-cells (autoimmune state). These models were able to explain cross-regulation deficits that lead to permanent autoimmune processes such as those happening on Lupus or type I Diabetes. Nevertheless relapsing-remitting dynamics of autoimmunity such as those found in Multiple Sclerosis still lack of a theoretical framework. In order to gain insights about the mechanisms that drive this relapsing-remitting dynamics, we have modeled the human adaptive immune system using a System Dynamics framework and stochastic differential equations. We hypothesized that the relapsing dynamics in autoimmunity can arise through a failure in the cross regulation mechanisms which control immune responses. The cross-regulation (Te-Treg loop) continuously faces stochastic events that activate the immune system (stochastic failure in central tolerance, stochastic activation by pathogens). The negative feedback loop between Treg and Te cells is essentially a prey-predator system where Te cells can be seen as prey and Treg cells as predators. The major contribution of the model introduced in this paper is a dynamical explanation of such relapsing-remitting dynamics. Hence our study provides a different point of view for relapse-remitting autoimmune disease and proposes new clues for the development of immunotherapies.

References:

- [1] Carneiro, J., et. al, T. 2007. When three is not a crowd: a Crossregulation Model of the dynamics and repertoire selection of regulatory CD4(+) T cells 6. Immunological Reviews 216:48-68.
- [2] Burroughs, et. al 2006. Regulatory T cell adjustment of quorum growth thresholds and the control of local immune responses. J. Theor. Biol. 241:134-141.

POSTERS

Título: *Gene expression analysis by game theory and microarray technology with an application in Autism Spectrum Disorder.*

Prof. Francisco J. Esteban

Department of Experimental Biology, University of Jaén and Center for Biomedical Informatics, Harvard Medical School, Boston (MA) &

Prof. Dennis P. Wall, Center for Biomedical Informatics, Harvard Medical School, Boston (MA)

Abstract: Microarray technology is a current approach for detecting alterations in the expression of thousands of genes simultaneously between two different biological conditions. Genes of interest are selected on the basis of an obtained p-value and, thus, the list of candidates may vary depending on the statistical test applied and data processing. Using this technology, several genes have been proposed as candidates in Autism Spectrum Disorder (ASD). However, and taking into account (i) the multifactorial character of ASD, (ii) the high inter-individual variability of the gene expression in ASD cases and (iii) the statistical analysis approach, sometimes is difficult and controversial to ascertain the differential gene expression in a given group of patients with ASD. Game theory has been recently proposed as a new method to detect the relevance of gene expression in different conditions. In this work, we apply the Shapley value to obtain the gene relevance on an ASD microarray data-set where only a few genes can be detected using conventional statistical approaches. The obtained results showed that coalitional games produced a significative increase in the number of genes that may be proposed to be involved in ASD. A further functional analysis demonstrated that groups of these genes were associated to biological functions and diseases previously related to ASD.

References:

[1] Moretti S, van Leeuwen D, Gmuender H, Bonassi S, van Delft J, Kleinjans J, Patrone F, Merlo DF. Combining Shapley value and statistics to the analysis of gene expression data in children exposed to air pollution, *BMC Bioinformatics* 9:361 (2008)

[2] Wall DP, Esteban FJ, Deluca TF, Huyck M, Monaghan T, Velez de Mendizabal N, Goñi J, Kohane IS. Comparative analysis of neurological disorders focuses genome-wide search for autism genes. *Genomics* 93:120-9 (2009)

Título: *Non-Intersecting Squared Bessel Paths and Multiple Orthogonal Polynomials for Modified Bessel Weights*

Prof. A. Martínez-Finkelshtein, Departamento de Estadística y Matemática Aplicada,, Universidad de Almería.

Abstract: We study a model of n non-intersecting squared Bessel processes in the confluent case: all paths start at time $t = 0$ at the same positive value $x = a$, remain positive, and are conditioned to end at time $t = T$ at $x = 0$. In the limit when n tends to infinity, after appropriate rescaling, the paths fill out a region in the t x -plane that we describe explicitly. In particular, the paths initially stay away from the hard edge at $x = 0$, but at a certain critical time t^* the smallest paths hit the hard edge and from then on are stuck to it. For $t = t^*$ we obtain the usual scaling limits from random matrix theory, namely the sine, Airy, and Bessel kernels. This is a joint work with A. B. J. Kuijlaars and F. Wielonsky.

PROGRAMA

Jueves, 12 de febrero de 2009

09:00 — 09:20 **Apertura**
09:30 — 10:30 Alberto Grünbaum
10:30 — 11:30 Alberto Grünbaum
11:30 — 12:00 **Café y discusión**
12:00 — 13:00 José Cuesta
13:00 — 14:00 José Cuesta
14:00 — 16:00 **Almuerzo y discusión**
16:00 — 17:00 Juan M.R. Parrondo
17:00 — 18:00 Franz Mertens
18:00 — 18:30 Luis Lafuente (25min + 5min de discusión)
18:30 — 19:00 Nieves Vélez (25min + 5min de discusión)
19:00 — 20:00 **Sesión de pósters y discusión**
21:30 — **Cena**

Viernes, 13 de febrero de 2009

09:30 — 10:30 Alberto Grünbaum
10:30 — 11:30 Alberto Grünbaum
11:30 — 12:00 **Café y discusión**
12:00 — 13:00 Juan M.R. Parrondo
13:00 — 14:00 Juan M.R. Parrondo
14:00 — 16:00 **Almuerzo y discusión**
16:00 — 17:00 José Cuesta
17:00 — 18:00 Jorge Zubelli
18:00 — 18:30 Jacobo Aguirre (25min + 5min de discusión)
18:30 — 19:00 José Ángel Capitán (25min + 5min de discusión)
19:15 — 20:45 **Excursión**
21:30 — **Cena**

Sábado, 14 de febrero de 2009

09:30 — 10:30 Juan M.R. Parrondo
10:30 — 11:30 Ana Nunes
11:30 — 12:00 **Café y discusión**
12:00 — 13:00 José Cuesta
13:00 — 14:00 Justo Puerto
14:00 — **Clausura, Almuerzo y discusión**

LISTA DE PARTICIPANTES

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