

# EVOLUTION of COMPLEX SYSTEMS



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Indian Institute of Science, Bangalore, India  
January 13 to 15, 2010

A PROGRAMME OF THE  
INTERNATIONAL CENTRE *for* THEORETICAL SCIENCES  
TATA INSTITUTE OF FUNDAMENTAL RESEARCH

Abstract Book

*EVOLUTION*  
*of*  
*COMPLEX SYSTEMS*

Indian Institute of Science  
Bangalore, India

January 13 to 15, 2010

**A Satellite Meeting of the ICTS Inaugural Event**



***Participating Institutions***

**SANTA FE INSTITUTE, SANTA FE, USA**

**INDIAN INSTITUTE OF SCIENCE, BANGALORE, INDIA**

**CENTRE FOR CELLULAR AND MOLECULAR BIOLOGY, HYDERABAD, INDIA**

# PROGRAMME

January 13

<b>Session I</b>	<i>Chairperson</i>	<i>Rahul Pandit</i>
<b>9:15</b>	<b>Spenta Wadia</b>	<b>Opening Remarks</b>
<b>9:30-10:15</b>	<b>Sriram Ramaswamy</b>	<b>The complex collective dynamics of self-driven particles</b>
<b>10:15-11</b>	<b>Upinder Bhalla</b>	<b>Multiple cellular states emerge from simple chemistry and cellular traffic</b>
<b>11-11:30</b>	<b>TEA</b>	
<b>11:30-12:15</b>	<b>Stefan Thurner</b>	<b>Darwin's daemon and a mechanistic approach to evolution dynamics</b>
<b>12:15-1</b>	<b>Bikas K Chakrabarti</b>	<b>Statistics of the Kolkata Paise Restaurant problem</b>
<b>1-2.45</b>	<b>LUNCH</b>	
<b>Session II</b>	<i>Chairperson</i>	<i>Sanjay Jain</i>
<b>2:45-3:30</b>	<b>Vidyanand Nanjundiah</b>	<b>The evolution of cooperation in social amoebae</b>
<b>3:30-4</b>	<b>TEA</b>	
<b>4-4:45</b>	<b>Anindita Bhadra</b>	<b>The links and hubs of power in a wasp society</b>
<b>4:45-5:30</b>	<b>R E Amritkar</b>	<b>Synchronization of networks</b>
<b>5:30-6:15</b>	<b>Sunil Kothari</b>	<b>New directions in Indian dance</b>
<b>6:15-7</b>	<b>TEA &amp; DISCUSSIONS</b>	
<b>8PM</b>	<b>DINNER</b>	

January 14

<b>Session III</b>	<i>Chairperson</i>	<i>Ravi Mehrotra</i>
<b>9:30-10:15</b>	<b>Didier Sornette</b>	<b>Black swans, Dragon-kings and predictions of crises in complex systems</b>
<b>10:15-11</b>	<b>Vikram Soni</b>	<b>Consequences of sudden species loss in an evolutionary model</b>
<b>11-11:30</b>	<b>TEA</b>	
<b>11:30-12:15</b>	<b>Neo Martinez</b>	<b>Structure, stability and robustness of complex ecological networks</b>
<b>12:15-1</b>	<b>Harini Nagendra</b>	<b>Charting the complexity of forest change in human impacted forests</b>
<b>1-2</b>	<b>LUNCH</b>	
<b>Session IV</b>	<i>Chairperson</i>	<i>Chandan Dasgupta</i>
<b>2-2:45</b>	<b>Priya Iyer</b>	<b>Theories for the evolution of the sexes</b>
<b>2:45-3:30</b>	<b>Amaresh Chakrabarti</b>	<b>Understanding and supporting evolution of engineering designs</b>

**TEA**

**K Ghosh Dastidar**

***On some aspects of price competition in a homogeneous product market: Evolution of cooperation, existence of equilibrium and other issues***

## Sanjay Jain

### ***Formalizing the notion of 'innovation' in an evolutionary model***

## TEA & DISCUSSIONS

***DINNER***

January 15

*Chairperson Somdatta Sinha*

**M. Madan Babu**

## ***Structure, evolution and dynamics of transcriptional regulatory networks and its influence on genome organization***

# Vijay Srinivasan

## ***Minimal metabolome: The canonical network of autotrophic metabolism and its analysis***

**TEA**

## Neelima Gupte

## Statistical characterisers of transport in communication networks

## Alain Pumir

## Quantifying complexity of genetic interactions: Theoretical analysis of Invertebrate phototransduction

**LUNCH**

*Chairperson Karmeshu*

## Sumantra Chattarji

## ***Differentiating safe from dangerous: From behavior to single neurons***

## G Rangarajan

## Detecting functional connectivity in neuronal networks

**TEA**

## Manindra Agrawal

## Classifying complexity of problems algorithmically

ORGANISERS

***Chandan Dasgupta***  
Department of Physics, Indian Institute of Science, Bangalore

***Raghavendra Gadagkar***  
Centre for Ecological Sciences Indian Institute of Science, Bangalore

***Somdatta Sinha***  
Centre for Cellular and Molecular Biology, Hyderabad

**Department of Physics, Indian Institute of Science, Bangalore**

**Centre for Ecological Sciences Indian Institute of Science, Bangalore**

**Centre for Cellular and Molecular Biology, Hyderabad**

## **The complex collective dynamics of self-driven particles**

***Sriram Ramaswamy***

Centre for Condensed Matter Theory, Department of Physics, Indian Institute of Science,  
Bangalore, India

I will discuss the dynamics of collections of self-propelled objects, as an interesting blend of agent-based flocking models and liquid crystal hydrodynamics. I will attempt to place the subject in a complex-systems context, and talk about some surprising experimental realizations.

## **Multiple cellular states emerge from simple chemistry and cellular traffic**

***Upinder S. Bhalla***

National Centre for Biological Sciences, Bangalore, India

The chemical environment in a cell is enormously complex, and typical systems biology analyses of cellular signaling reveal hundreds of interacting molecular species. How do such systems self-organize? One important aspect of cellular function is the ability of the cell to adopt different states at different times, and in different places within the cell. For example, the molecular identity of each cellular organelle is defined by its adopting a state having a certain molecular composition, and sustaining this state despite ups and downs in cellular metabolism. Multi-stable chemical circuits exhibit a similar capability of sustaining distinct states. We have used mass-action kinetic simulations to investigate multi-stability in tens of thousands of simple chemical systems, and find that multi-stability is remarkably common. Furthermore, multi-stable systems are closely related to each other, suggesting that this may be a good substrate for evolution of more complex and regulated multi-stable switches. We have extended stability analysis to look at multi-compartmental systems undergoing cell-biologically important processes such as molecular traffic. We find that many combinations of trafficking and chemical signaling give rise to multi-stable systems spanning compartments, with as many as four stable states. Together these results suggest that key aspects of cellular function may self-organize out of relatively simple chemical processes. Evolution may be able to achieve many kinds of cellular organization and control based on some of these common principles.

## **Darwin's daemon and a mechanistic approach to evolution dynamics**

***Stefan Thurner***

Complex Systems Research Group, Medical University of Vienna, Austria,  
External Professor,  
Santa Fe Institute, USA

An essential characteristic of evolutionary systems is its ongoing and endogenous production of new species, goods, services, etc. These novel entities change the conditions for proliferation or (re)production of already existing entities. In other words, the fitness landscape co-evolves as a function of the diversity of the system. We propose a simple model for evolutionary systems, co-evolving with their fitness landscapes. On its basis, we are able to understand and predict several statistical and systemic features of evolutionary systems. Results can be compared to time series characteristics from systems ranging from the fossil record to macroeconomic economic instruments. We comment on a novel way of interpreting systemic risk in evolutionary systems.

## Statistics of the Kolkata Paise Restaurant problem

**Bikas K Chakrabarti**

Centre for Applied Mathematics & Computational Science, Saha Institute of Nuclear Physics & Economic Research Unit, Indian Statistical Institute, Kolkata, India

We study the dynamics of a few stochastic learning strategies for the “Kolkata Paise Restaurant” (KPR) problem [1, 2, 3], where  $N$  agents choose among  $N$  equally priced but differently ranked restaurants every evening such that each agent tries get to dinner in the best restaurant (each serving only one customer and the rest arriving there going without dinner that evening). We consider the learning strategies to be similar for all the agents and assume that each follow the same probabilistic or stochastic strategy dependent on the information of the past successes in the game. The numerical results for utilization of the restaurants in some limiting cases are analytically examined.

Let the symmetric stochastic strategy chosen by each agent be such that at any time  $t$ , the probability  $p_k(t)$  to arrive at the  $k$ -th ranked restaurant is given by

$$p_k(t) = \frac{1}{Z} \left[ k^\alpha \exp \left( -\frac{n_k(t-1)}{T} \right) \right], Z = \sum_{k=1}^N \left[ k^\alpha \exp \left( -\frac{n_k(t-1)}{T} \right) \right], \quad (1)$$

where,  $n_k(t)$  denotes the number of agents arriving at the  $k$ -th ranked restaurant in period  $t$ ,  $T > 0$  is a scaling factor and  $\alpha \geq 0$  is an exponent. We consider the KPR problem where the decision made by each agent in each time period  $t$  is independent and is based on the information about the rank  $k$  of the restaurants and their occupancy given by the numbers  $n_k(t-1) \dots n_k(0)$ . We consider several stochastic strategies where each agent chooses the  $k$ -th ranked restaurant with probability  $p_k(t)$  given by Eq. (1).

The utilization fraction  $f_k$  of the  $k$ -th ranked restaurants on every evening is studied and their average (over  $k$ ) distributions  $D(f)$  for some special cases. From numerical studies, we find their distributions to be Gaussian with the most probable utilization fraction  $\bar{f} \simeq 0.63, 0.58$  and  $0.46$  for the cases with  $\alpha = 0, T \rightarrow \infty$ ;  $\alpha = 1, T \rightarrow \infty$ ; and  $\alpha = 0, T \rightarrow 0$  respectively. For the stochastic crowd-avoiding strategy, we get the best utilization fraction  $\bar{f} \simeq 0.8$ . The analytical estimates for  $\bar{f}$  in these limits are also given and they agree very well with the numerical observations.

Also, we suggest ways to achieve the ideal social norm either exactly in the presence of incentive problem or asymptotically in the absence of such incentive problem. Implementing or achieving such a norm in a decentralized way is impossible when  $N \rightarrow \infty$  limit. The KPR problem has similarity with the Minority Game Problem as in both the games, herding behavior is punished and diversity is encouraged. Also, both involve learning of the agents from the past successes etc. Of course, KPR has some simple exact solution limits, a few of which are obvious. In none of these cases considered so far, learning strategies are individualistic; rather all the agents choose following the probability given by Eq. (1). In a few different limits of such a learning strategy, the average utilization fraction  $\bar{f}$  and their distributions are obtained and compared with the analytic estimates, which are reasonably close. Needless to mention, the real challenge is to design algorithms of learning mixed strategies (e.g., from the pool discussed here) by the agents so that the ideal social norm emerges eventually even when everyone decides on the basis of their own information independently.

It may be noted that all the stochastic strategies, being parallel in computational mode, have the advantage that they converge to solution at finite steps (independent of  $N$ ) while for deterministic strategies the convergence time is typically of order of  $N$ , which renders such strategies useless in the truly macroscopic ( $N \rightarrow \infty$ ) limits. However, deterministic strategies are useful when  $N$  is small and rational agents can design appropriate punishment schemes for the deviators.



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## **The evolution of cooperation in social amoebae**

***Vidyanand Nanjundiah***

Centre for Ecological Sciences, Indian Institute of Science & Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, India

Amoebae belonging to the Dictyostelid or cellular slime moulds display a transition from solitary to social behaviour during their life cycle. The social phase is characterized by an extreme form of cooperation with division of labour; some cells display traits that appear to aid the survival and reproduction of other cells while lowering their own fitness. Phenomena such as this, often described as 'altruism', have puzzled evolutionary biologists ever since Darwin drew special attention to them in *The Origin of Species*. This talk will attempt to make a case for a pluralistic approach to understanding the evolution of 'altruistic' behaviour, both in general and in the cellular slime moulds in particular. It will be suggested that non-genetic variation between single cells plays an important role in their division of labour.

## **The links and hubs of power in a wasp society**

***Anindita Bhadra***

Behaviour and Ecology Lab, Dept. of Biology,  
Indian Institute of Science Education and Research,  
Mohanpur, West Bengal, India

Insect societies serve as excellent model systems for understanding the causes of conflict and the evolution of cooperation in the living world. Highly evolved social insects like the honey bees and ants typically have colonies headed by morphologically distinct queens and are considered as the pinnacles of social organization. In the so-called primitively eusocial species, on the other hand, the queens are not morphologically distinguishable from the workers, and caste is determined mostly through social interactions. The queens in these species are typically the most aggressive individuals, who are believed to use physical aggression to maintain reproductive monopoly as well as to regulate worker activities in the colony. The paper wasp *Ropalidia marginata* is an excellent system for studying the process of social evolution. While *R. marginata* is characterized as primitively eusocial due to the lack of a morphologically distinct queen, this species displays many features of highly evolved societies, the most notable being the absence of a physically aggressive queen. How does such a docile queen maintain reproductive monopoly in the colony? How is work regulated in the colony? How is the queen's successor determined? These are some of the most intriguing questions that can be asked about this species. While behavioural studies have been used for many years to address these questions, social network analysis now lends support to our earlier observations, enhancing our understanding of the social biology of *R. marginata*.

## **Synchronization of networks**

***Ravindra E. Amritkar***

Physical Research Laboratory, Ahmedabad, India

Synchronized behavior of a network of interacting dynamical systems or oscillators is a commonly observed phenomena. Synchronization of time varying networks is possible and its stability properties are decided by the commuting or noncommuting nature of the coupling matrices.

In the context of many biological systems such as coupled neurons, synchronous behaviour can occur due to interaction through a common chemical medium. We consider synchronization of chaotic oscillators coupled via feedback with a dynamic environment and show that both anti-phase and in-phase synchronization are possible.

There are several applications of network synchronization and one interesting application is for the extinction of species. It can be shown that the species will show spatial synchronization of populations before extinction. This may explain the absence of the 'rescue effect' in the extinction of species.

## **New directions in Indian dance**

***Sunil Kothari***

School of Arts and Aesthetics, Jawaharlal Nehru University, New Delhi, India  
Visiting Professor: Tisch School of Arts, New York University, New York, USA

Classical Indian Dance forms have a complex structure, a grammar, and a system of transmitting techniques. Evolved over several centuries, with a text like Natyashastra (2nd century BC -4th century AD), and other texts, manuals, it constantly evolves and is never static.

Creative dancers like Uday Shankar and his associates, the moderns like Poet Rabindranath Tagor, Vallathol, Rukmini Devi Arundale, Madame Menaka, RamGopal, Mrinalini Sarabhai, Chandralekha, Kumudini Lakhia, Manjushri Chaki Sircar, and others have, after mastering classical dance techniques, evolved their own techniques rooted deeply in tradition, but bringing in contemporary sensibilities and addressing contemporary issues, bringing dance closer to life their works.

The talk will discuss these issues with excerpts form the choreographic works of Uday Shankar, Chandralekha, Kumudini Lakhia, Aditi Mangaldas, Priti Patel, Daksha Seth, and few Indian Diaspora dancers.

## **Black Swans, Dragon-kings and predictions of crises in complex systems**

***Didier Sornette***

Department of Management, Technology and Economics, ETH Zurich,  
Zurich, Switzerland

Extreme fluctuations or events are often associated with power law statistics. Indeed, it is a popular belief that "wild randomness" is deeply associated with distributions with power law tails characterized by small exponents. In other words, power law tails are often seen as the



epitome of extreme events. Here, we document in many different systems that there is life beyond power law tails: power laws can be superseded by "dragon-kings", monster events that occur beyond the power law tail. Dragons reveal hidden mechanisms that are only transiently active and that amplify the normal power law fluctuations. We will present evidence of the dragon-king phenomenon on the statistics of financial losses, economic geography, hydrodynamic turbulence, material rupture, earthquakes, epileptic seizures, and cyber risks. The special status of dragon-kings open a new research program on their predictability, based on the hypothesis that they belong to a different class of their own and express specific mechanisms amplifying the normal dynamics via positive feedbacks. We will present evidence of these claims for the predictions of material rupture, financial crashes and epileptic seizures. The dragon-king approach allows us to understand the present World financial crisis as underpinned by two decades of successive financial and economic bubbles. We will demonstrate how market risk management can be enlarged by combining strategic, tactical and time-varying risk analysis.

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## Consequences sudden species loss in an evolutionary model

**Vikram Soni**

Centre for Theoretical Physics, Jamia Millia Islamia, New Delhi, India

According to the IUCN and millennium reports, in the last 50 years, 30% of the species in the sea and on land are facing extinction. In terms of evolutionary time, this is a sudden loss. In a simplified model of an evolutionary network, we look at a sudden (random) cut in the number of species and the probability of a crash of the network, where a crash is defined as 75% of the species depopulating or going extinct. Our findings indicate that for a 20%, 30%, 40% sudden species loss the probability of a network crash is ~30%, ~60%, ~90%.

## Structure, Stability and Robustness of Complex Ecological Networks

**Neo Martinez**

Pacific Ecoinformatics and Computational Ecology Lab Berkeley, California, USA

"It is interesting to contemplate a tangled bank, clothed with many [species] of many kinds, ... so different from each other, and dependent upon each other in so complex a manner, have all been produced by laws acting around us." "Origin of Species" Darwin (1859)

The science of complex networks is one of the most exciting research areas of systems sciences including complexity research, social network analysis and systems biology. Nowhere is this more apparent than in ecology. Research on complex ecological networks, which Darwin famously depicted as a "tangled bank" 150 years ago, has recently discovered how incredibly complex ecosystems made up of spectacularly diverse and highly interdependent species remain surprisingly stable. Even more recently, scientists have applied this research to understanding resistance, robustness and resilience of ecosystems to disturbances such as species loss and invasion. This work has many lessons for network science in general and the integration of ecology with human systems. This ongoing research will be presented along with the visual and computational analyses responsible for the findings and future directions of this field.

### **Charting the complexity of forest change in human-impacted forests**

***Harini Nagendra<sup>1,2</sup> and Elinor Ostrom<sup>3,4</sup>***

<sup>1</sup>Ashoka Trust for Research in Ecology and the Environment, Bangalore, India

<sup>2</sup>Center for the Study of Institutions, Population, and Environmental Change, Indiana University, USA

<sup>3</sup>Workshop in Political Theory and Policy Analysis, Indiana University, USA

<sup>4</sup>Center for the Study of Institutional Diversity, Arizona State University, USA

Current research on forest change takes into consideration a variety of measures of forest conditions. These range from quantitative assessments of variables such as extent, density, diversity, and biomass, to more qualitative and integrated estimates of forest condition provided by foresters and users. Yet, very few studies of forests examine the change in forest conditions – yet, such assessments are critically needed so as to assess the consequences of institutional arrangements, economic pressures, or local organization. The International Forestry Resources and Institutions research program, spread across 11 countries, records a variety of measures of forest condition at repeated intervals of time. Using a dataset of 59 forests from 5 countries - Nepal, India, Kenya, Uganda and the USA - we compare multiple indicators of forest change. Our findings point clearly to the complexity of human-impacted forests, which demonstrate considerable variation in different aspects. Developing a single index of forest change that indicates whether a forest is deteriorating or improving over time is a very challenging task. Instead, forests need to be more appropriately viewed as complex systems whose evolution can take them in different directions, depending on local and regional constraints and opportunities. Especially in light of current discussions on climate change and forest governance, these issues need to be highlighted and discussed as a foundation for future research and analysis into the dynamics of forest change.

### **Theories for the evolution of the sexes**

***Priya Iyer***

Indian Institute of Science Education and Research, Pune, India

This talk is about the evolution of male and female and the differences between them, especially in the animal kingdom. Ideas of sex-specific templates and conflict between the male and female strategies go back to Darwin and have been used to explain the evolution of differences between the sexes since their origin in the form of small sperm and large eggs. However, numerous morphs and behaviours across species serve as exceptions to the

prescribed templates, and many empirical studies disagree with key predictions of the prevalent theories based on conflict. As an alternative, I propose that the fundamental differences between the sexes evolved to increase the fitness of both sexes by virtue of specialization. Hence small sperm and large eggs increase contact rates as well as zygote viability, and dioecy may evolve as a specialization to increase the efficiency of offspring production. Alternative hypotheses to explain the diversity in morphologies and behaviours may be developed by allowing for more complex behavioral dynamics, and hence a departure from traditional evolutionary game theory. I illustrate one such hypothesis pertaining to the evolution of showy ornaments, which are often conspicuously different between the sexes, and suggest how it may be tested. Directions for future research include development of theory for the evolution of such complex societies.

## **Understanding and supporting evolution of engineering designs**

***Amaresh Chakrabarti***

Centre for Product Design and Manufacturing,  
Indian Institute of Science, Bangalore, India

By designs, we mean plans which when implemented and utilized as intended, are meant to serve some goals - changes from some current, undesired situation into some future, desired situation. Designing is the process through which designs are developed. Design and designing – in this broad sense involves all intentional acts of creation with goals – be they paintings, advertisements, theories, or technical systems. Technical systems transform energy, materials and signals for solving societal problems.

The talk will introduce our work on understanding how the generic act of designing of technical systems takes place - how engineering design ideas evolve from the imprecise and incomplete perceived descriptions of intent and problems to become concrete and detailed physical structures that can be implemented and utilized as intended.

We carry out these studies using multiple techniques, the most detailed being video protocol analysis where problem solving sessions of designers and design teams are audio-videotaped to identify the utterances, gestures and physical actions carried out by the them to understand how these complex systems - the designs - evolve.

As part of this work, we have developed a “GEMS of SAPPhIRE” model of conceptual designing that helps us ask the question: how do designers develop designs? The model is based on the “SAPPhIRE” Model of causality that we had developed earlier for explaining how systems work. The model has been empirically tested in that all constructs of the model are naturally present in all acts of technical designing we observed, and none other than those anticipated in the model.

When a process of designing is analyzed using the model, it helped us identify some crucial gaps in how designers currently develop these systems, particularly from the point of view of novelty of designs produced – a primary attribute of interest for technical innovation. This provided directions in which to modify these processes so as to support designers develop substantially novel designs.

## **On some aspects of price competition in a homogeneous product market: Evolution of cooperation, existence of equilibrium and other issues**

***Krishnendu Ghosh Dastidar***

Centre for Economic Studies and Planning  
School of Social Sciences, Jawaharlal Nehru University,  
New Delhi, India.

We consider a simultaneous move price choice game in a homogeneous product oligopoly where there are  $n$  firms. All firms have identical cost functions. Firms simultaneously and independently quote prices. The firm quoting the lowest price gets the entire demand. If there is a tie at the lowest price, then we assume that all the firms tied at the lowest price share the demand equally. We will also assume that a firm always meets the demand it faces at the posted price. In this framework, we discuss the following:

1. Existence and nature of Bertrand equilibria both with and without capacity constraints. Here we illustrate “Bertrand Paradox” and the possible ways to resolve this;
2. In a dynamic (infinitely repeated game theoretic) context, we show how cooperation can be achieved through non-cooperative interaction;
3. We show how the theory can be very useful in explaining some real life issues like “price wars during booms”.

## **Formalizing the notion of ‘innovation’ in an evolutionary model**

***Sanjay Jain***

Department of Physics and Astrophysics,  
University of Delhi;  
JNC SAR, Bangalore;  
Santa Fe Institute, Santa Fe, New Mexico, USA

‘Innovations’ are central to the evolution of societies and the evolution of life, but we do not have an analytical framework for describing them. Innovations occur in every sphere of human activity – in the artifacts that humans build, in the world of ideas, and in the organization of society. They also occur in contexts removed from the human; for example, we say in biology that the emergence of photosynthesis, multicellularity, and the eye are examples of evolutionary innovation. Innovations seem to naturally arise in complex evolving systems, and their appearance is a crucial driving force in the subsequent evolution of these systems.

Which events or sets of events deserve to be called ‘innovation’? After the event, when its impact or consequences are known we can often agree that something was an innovation, and even on whether it was a ‘big’ innovation or a ‘small’ one. But can we recognize an innovation as it appears, ‘on the fly’? Successful entrepreneurs sometimes can. Can we formalize that intuition? Do innovations have a special ‘structural’ character with respect to the existing context?

In this talk I would like to describe a mathematical example of an evolving complex system that exhibits events that seem to qualify as (very rudimentary) innovations. The model is motivated by the origin of life problem and describes an idealized prebiotic network of interacting molecules. The network changes as new molecules arrive in the system and existing ones get eliminated as their population depletes. The evolution of the system shows repeated rounds of random evolution followed by self-organization and growth of structure, stasis,

collapse, recovery, re-collapse, etc. These transformations are triggered by events in which new molecules link up with existing ones in a special manner. An innovation is an event that forges new relationships between existing structures, relationships that can be recognized as special and that produce a new structure with a potential to transform the subsequent evolution. There turn out to be different classes of new relationships that arise in the model; these can be mathematically characterized in structural terms, and they correspond to different kinds of innovation, big and small.

## **Structure, evolution and dynamics of transcriptional regulatory networks and its influence on genome organization**

***M. Madan Babu***

MRC Laboratory of Molecular Biology, Cambridge, UK  
Fellow of Darwin College, Cambridge, UK

The availability of entire genome sequences and the wealth of literature on gene regulation have enabled researchers to model an organism's transcriptional regulation system in the form of a network. In such a network, transcription factors or target genes are represented as nodes and regulatory interactions are represented as directed edges. In this talk, I will address the following aspects of transcriptional regulatory networks: (i) Structure and organization: I will first provide an introduction to the concept of networks and discuss our current understanding of the structure and organisation of transcriptional networks. (ii) Evolution: I will then describe the different mechanisms and forces that influence network evolution and shape network structure. In particular, I will talk about the impact of evolutionary mechanisms such as gene duplication, gene gain and loss and that of the environment on transcriptional network evolution. (iii) Dynamics: Here, I will discuss studies that have integrated information on dynamics such as mRNA abundance, half-life, etc with data on transcriptional network in order to elucidate general principles that we know of regulatory network dynamics. In particular, I will discuss how cell to cell variability in the levels of transcription factors could permit differential utilization of the same underlying network by distinct members of a genetically identical cell population. (iv) Impact on genome organization: Finally, I will discuss how the various aspects of transcriptional regulation discussed above could possibly influence genome organisation. In particular, I will talk about how they could have influenced the way in which genes are organised on chromosomes. Finally, the implications of these new concepts for microbial pathogenesis, synthetic biology, microbial engineering will also be discussed.

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### **Minimal metabolome: The canonical network of autotrophic metabolism and its analysis**

***Vijay Srinivasan***

Krasnow Institute for Advanced Study,  
George Mason University, Fairfax, VA, USA

Prebiotic chemistry required the availability and selection of metabolic compounds that were organized into molecular networks resulting in the emergence of intermediary metabolism – a phenomenon which is the foundation and the first level in biological emergence. Autotrophs, especially reductive chemoautotrophs are now believed by many to be the earliest cellular forms. In our quest towards understanding selection principles in biogenesis, we reconstructed the canonical network of autotrophic metabolism that represents the minimal metabolome of a reductive autotroph. Compounds of this anabolic network were classified into different groups based on their nodal status in the network. To aid in the analysis of the network, the metabolic chart was deconstructed into a core and other subgraphs. Analysis of the core sub-network showed several empirical generalizations, which include a complete utilization of reaction outputs with no molecules left behind thus ensuring a total conservation of information. This and other generalizations that emerged including network robustness and the structural hierarchy, sparseness in both the core set of compounds and in the types of chemicals reactions that generated them will be discussed.

The central feature of an autotroph is its ability to synthesize all compounds of intermediary metabolism exclusively from inorganic sources utilizing CO<sub>2</sub> as the single reservoir of carbon. Literature survey of experimental autotrophs reveals the addition of extraneous vitamins and organic metal ion chelators to the growth media, which may compromise this critical attribute and thus raise queries on the definition and identity of a true autotroph. This leads to addressing the essentiality and the central role of transition metals in the origin and evolution of life, an issue that has received very little attention. We are currently studying the role of transition metals in biogenesis.

### **Statistical characterisers of transport in communication networks**

***Neelima M. Gupte***

Department of Physics  
Indian Institute of Technology, Chennai 600036, India

## **Quantifying complexity of genetic interactions: Theoretical analysis of invertebrate phototransduction**

***Alain Pumir<sup>1</sup> and Boris I Shraiman<sup>2</sup>***

<sup>1</sup>Laboratoire de Physique,  
Ecole Normale Supérieure de Lyon, Lyon, France.

<sup>2</sup>Kavli Institute for Theoretical Physics and Department of Physics, University of California,  
Santa Barbara, CA, USA

Biological functions are performed by complex molecular networks involving many feedback and regulatory interactions. Genetic variation in natural populations implies variation in the biochemical parameters of the protein components of these networks and it is important to understand the effects that such variation has on their function. It is often assumed that the effects of genetic variation at multiple loci (i.e. in multiple genes) are additive. Yet more generally one expects the effect of allelic variation at one locus to depend on the genetic background (i.e. on the alleles at other relevant loci). To date, properly quantifying this non-additivity - known as epistasis in population genetics - in an experimental systems remains a difficult task.

Here, I will discuss the expected general nature of interaction between components of realistic biological systems with the help of a recently developed model of invertebrate phototransduction<sup>1</sup>. In phototransduction a single photon induces a transient electrical depolarization of the photoreceptor cell, known as 'quantum bump'. The model reproduces quantitatively the 'all-or-none' response of the system and provides a detailed description of the properties of the QBs when the parameters of the system are varied. The response of the system depends on a number of parameters, which we associate with a part of the underlying molecular network. We establish the mapping between the model parameters and the systems response, which can be interpreted as genotype-to-phenotype relation, and propose a decomposition that properly separates the additive part and the pair, triad and higher order interactions within the network. Even for a highly nonlinear system, such as invertebrate phototransduction, the additive part is found to be the dominant one. Interaction being most components of the network is comparatively very weak, except for relatively rare sets of components. Our analysis allows us to distinguish between non-interactive parts of the network, and functionally connected part. The analysis presented here provides a theoretical framework to analyze the experimental data, and to clarify the role of interaction between components in complex biological system.

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## **Differentiating safe from dangerous: from behavior to single neurons**

***Sumantra Chattarji***

National Centre for Biological Sciences, TIFR, Bangalore, India

One of the most powerful model systems for elucidating the neural basis of learning has been auditory fear conditioning, in which subjects rapidly learn to associate a previously neutral tone (CS, conditioned stimulus) with a coincident aversive stimulus (US, unconditioned stimulus), e.g. a foot shock. Re-exposure to the CS alone elicits a conditioned response — "freezing", which provides a measure for the learned association. The early stages of fear



memory formation involve strengthening of sensory afferents from the thalamus to the amygdala, a brain structure that plays a pivotal role in emotional information processing. As useful as this simple behavioral model has been in studying basic cellular mechanisms of associative learning, it does not capture some of the essential features of learning in the “real world”. A fundamental challenge, from a computational point of view, is that learned associations are rarely invariant over time and need to be generalized appropriately to novel settings. There are costs associated with both too little and too much generalization and appropriate generalization is, thus, necessary for survival. Understanding these processes is also critical for gaining insights into affective disorders such as post-traumatic stress disorder (PTSD), which may be viewed as an instance of overgeneralization. I will present experimental data on the encoding of fear generalization in awake, behaving rats at the level of single amygdala neurons. Our findings identify novel neural mechanisms that may provide insights into the transition of emotional states from normal fear to pathological anxiety exhibited in stress disorders.

### **Detecting functional connectivity in neuronal networks**

***Govindan Rangarajan***

Department of Mathematics, Indian Institute of Science, Bangalore, India

Detecting functional connectivity between different regions of a neuronal network has become increasingly important. Changes in functional connectivity between different brain regions can serve as a functional biomarker for early detection of neuro-degenerative diseases such as Alzheimer's disease. Granger causality can be used to detect functional connectivity. But a good fraction of the data from neuroscience experiments is in the form of spike train data, which needs to be modeled using point processes. Classical Granger causality, however, is not applicable to point processes. We therefore extend Granger causality to point processes using spectral factorization. We then apply this to both simulated and experimental data. If time permits, we will also describe a new concept called block coherence, which we have developed to determine coherence between two brain regions. This serves as another method to detect functional connectivity.

### **Classifying complexity of problems algorithmically**

***Manindra Agrawal***

Department of Computer Science and Engineering, Indian Institute of Technology, Kanpur, India

Algorithms provide a nice framework to classify the complexity of problems: the complexity of a problem is defined to be the amount of resources, typically time and / or space, required to solve the problem algorithmically. This captures, in a strong sense, our intuition about the complexity of a problem. For example, the problem of adding two numbers is intuitively easier than the problem of multiplying two numbers and this is borne out by the time taken by the respective algorithms to solve them. In this talk, I will introduce the notions of time and space complexity of problems, discuss relationships between them, define some important classes of problems, and discuss the complexity of several well-known problems.

## **List of Speakers**

### **Manindra Agrawal**

Dept. of Computer Science and Engineering,  
Indian Institute of Technology Kanpur, India

### **R E Amritkar**

Physical Research Laboratory, Ahmedabad  
380009, India

### **Anindita Bhadra**

Behaviour and Ecology Lab, Dept. of Biology,  
Indian Institute of Science Education &  
Research, Mohanpur, WB

### **Upinder Bhalla**

National Centre for Biological Sciences,  
TIFR, Bangalore, India

### **Amaresh Chakrabarti**

Centre for Product Design and  
Manufacturing, Indian Institute of Science,  
Bangalore, India

### **Bikas K Chakrabarti**

Centre for Appl. Maths. & Computational  
Science, Saha Institute of Nuclear Physics,  
Kolkata, & ERU, Indian Statistical Institute,  
Kolkata, India

### **Sumantra Chattarji**

National Centre for Biological Sciences,  
TIFR, Bangalore, India

### **Krishnendu Ghosh Dastidar**

Centre for Economic Studies and Planning,  
School of Social Sciences,  
Jawaharlal Nehru University, New Delhi

### **Neelima M. Gupte**

Department of Physics, Indian Institute of  
Technology, Chennai 600036

### **Priya Iyer**

Indian Institute of Science Education and  
Research, Pune

### **Sanjay Jain**

Physics Department,  
University of Delhi, Delhi, India

### **Sunil Kothari**

School of Arts and Aesthetics, Jawaharlal  
Nehru University, New Delhi; Visiting  
Professor, Tisch School of Arts, New York  
University, NY, USA

### **M. Madan Babu,**

MRC Laboratory of Molecular Biology,  
University of Cambridge, Cambridge, UK

### **Neo Martinez**

Pacific Ecoinformatics and Computational  
Ecology Lab, Berkeley, California, USA;  
Santa Fe Institute, Santa Fe, New Mexico,  
USA

### **Harini Nagendra,**

Ashoka Trust for Research in Ecology and  
the Environment, Bangalore, India;  
Center for the Study of Institutions,  
Population, and Environmental Change,  
Indiana University, USA

### **Vidyanand Nanjundiah,**

Centre for Ecological Sciences, Indian  
Institute of Science, and Jawaharlal Nehru  
Centre for Advanced Scientific Research,  
Bangalore, India

### **Alain Pumir**

Laboratoire de Physique, Ecole Normale  
Supérieure de Lyon, F - 69007,  
Lyon, France.

### **Sriram Ramaswamy**

Centre for Condensed Matter Theory,  
Department of Physics,  
Indian Institute of Science, Bangalore, India

### **G Rangarajan,**

Department of Mathematics,  
Indian Institute of Science, Bangalore, India

### **Vikram Soni**

Centre for Theoretical Physics,  
Jamia Millia Islamia,  
New Delhi, India

**Didier Sornette**

Department of Management, Technology and  
Economics, ETH Zurich, Zurich, Switzerland

**Vijay Srinivasan**

Krasnow Institute for Advanced Study,  
George Mason University, VA 22030, USA

**Stefan Thurner**

Complex Systems Research Group, Medical  
University of Vienna, Austria, and External  
Professor, Santa Fe Institute, USA