Gregory Batt
A general computational method for robustness analysis with applications to synthetic gene networks

The robustness of biological systems behaviors has been demonstrated many times both experimentally and theoretically. In most cases however, the definition of robustness is highly problem-dependent, if not purely informal. An interesting general formal definition of robustness has recently been given by H. Kitano [Mol.Syst.Biol, 2007]. The robustness of a property with respect to a set of perturbations is the average value of the functionality of the system under all perturbations, weighted by the perturbation probabilities. Unfortunately, no indications are given on how to define and quantify the ``functionality'' of a system.

Here, we propose an instantiation of this abstract definition, and an effective procedure to estimate it computationally. In this setting, the expected behavior is given as a temporal logic specification, and the behavior of the system under perturbations is simply given by a set of numerical traces. Our technique is rather general since most modeling formalisms provide numerical traces as simulation results and since temporal logics are versatile specification languages adapted to capture the quantitative yet imprecise aspects of cellular behavior. The computation of the robustness estimate is based on the notion of violation degree that measures the distance between the expected behavior and the behavior of the perturbed system [Rizk et al, CMSB'08]. This method has been implemented in the modeling environment Biocham and applied to cell cycle and transcriptional cascade models.

Joint work with Aurélien Rizk, Sylvain Soliman and François Fages (Contraintes, INRIA)

Bud Mishra
Algebra, Automata, Algorithms, Biology and Beyond

In this talk, I will introduce a new approach to modeling dynamics of biological systems and its relations to certain problems in algebra and algorithmics: namely, decision procedures for systems of linear Diophantine equations and inequalities, whose coefficients range over algebraic numbers and intervals. The questions, addressed here, are central to the success of the emerging field of systems biology and relate to questions in decidability theory, algorithmic algebra, hybrid automata models, etc.

Radu Grosu
Spatial Abstraction in Reaction-Diffusion Systems

The automatic verification of biological systems (BS) poses significant challenges due to their nonlinear dynamics, mixed discrete-continuous and possibly stochastic behavior, and spatial distribution. Each of these features alone may render the analysis of a BS intractable. The hybrid-systems (HS) community has focused so far on developing tools and techniques that make it possible to perform temporal-logic model checking of HS modeled as automata with linear dynamics. Biological systems however, prominently feature a spatial dimension. Consequently, checking that a BS satisfies a spatial-temporal property is beyond the reach of current HS verification technology. In previous work we developed a spatial-superposition abstraction and associated logic which allowed us to check if an emergent spatial property holds in a particular state of a network of interacting hybrid automata (modeling cardiac tissue). In this talk we discuss spatial-temporal abstraction techniques that would enable the verification of spatial-temporal properties of biological systems.

Ashish Tiwari
Analyzing the Aplysia Central Pattern Generator

Aplysia is a marine mollusk that is a useful animal model system for investigating neural circuit functions. The feeding behavior of Aplysia is well studied and the neural circuit responsible for mediating the rhythmic movements of its foregut during feeding has been identified. This rhythmic behavior is generated by a central pattern generator (CPG) located in the buccal ganglia of *Aplysia*. How this neural circuit generates different behaviors, such as egestion and ingestion, and how it exhibits learning and memory are important questions that are now being answered by building and analyzing models of the neural circuits.

In this talk, we start with the continuous dynamical model for pattern generation underlying fictive feeding in *Aplysia* proposed by Baxter et.al.[Baxter06]. We then obtain a discrete model as a composition of discrete models of ten individual neurons in the CPG. The individual neurons are inter-connected through excitatory and inhibitory synaptic connections and electric connections. We use Symbolic Analysis Laboratory (SAL) to formally build the model and analyze it using the SAL model checker. Using abstract discrete models of the individual neurons helps in understanding the buccal motor programs generated by the neural network in terms of the network connection topology. It also eliminates the need for detailed knowledge of the unknown parameters in the continuous model of Baxter et.al.[Baxter06].

Eugenio Cinquemani
Stochastic dynamics of genetic regulatory networks: Modeling and identification

Genetic regulatory networks govern the synthesis of proteins in the living cell and are thus responsible for fundamental cell functions such as metabolism, development and replication. Genetic network modeling has been mostly developed in terms of either purely continuous or purely discrete dynamics. However, it appears that certain processes are more naturally described by models that feature both continuous evolution and discrete events. In addition, it is being recognized that many biological processes are intrinsically uncertain.

In this talk I will discuss modeling and identification of genetic regulatory networks in a stochastic hybrid framework. A piecewise deterministic model is considered where the deterministic evolution of protein concentration levels is driven by the random activation and deactivation of gene expression. In turn, gene expression follows the laws of a finite Markov chain whose transition rates depend on the current protein concentrations. This modeling framework provides a convenient tradeoff between accuracy and tractability and is well suited for genetic network analysis and model identification/validation.

Based on this framework, I will discuss identification of the regulatory network. I will consider the parameter estimation problem, where the interaction pattern of the network is assumed to be known. I will describe an estimation procedure that allows for the separate identification of the dynamics of every gene from sparse and noisy measurements of the protein concentration levels. This procedure scales well with the size of the network and is therefore applicable to networks of realistic size. Results from numerical experiments will be shown to discuss the performance of the method. To conclude, I will discuss current efforts addressing the structure identification problem, i.e. the problem of determining the network of interconnections among genes from experimental data.

Calin Belta
Formal approaches to analysis and synthesis of gene networks

I will show how a particular approach to modelling, together with discrete abstractions and model checking, can be used to tune and analyze gene networks from qualitative specifications given as arbitrary temporal and logic statements over species concentrations. I will exemplify the methods on two synthetic circuits: a four-gene transcriptional cascade and a two-gene toggle switch.

Emanuela Merelli
Model Checking Biological Oscillators

We define a subclass of timed automata, called oscillator timed automata, suitable to model biological oscillators. The semantics of their interactions, parametric with respect to a model of synchronization, is introduced. We apply it to the Kuramoto model. Then, we introduce a logic, Kuramoto Synchronization Logic (KSL), and a model checking algorithm in order to verify collective synchronization properties of a population of coupled oscillators.