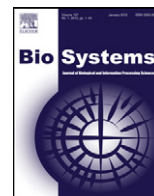




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## Computational models of signalling networks for non-linear control

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### ABSTRACT

Artificial signalling networks (ASNs) are a computational approach inspired by the signalling processes inside cells that decode outside environmental information. Using evolutionary algorithms to induce complex behaviours, we show how chaotic dynamics in a conservative dynamical system can be controlled. Such dynamics are of particular interest as they mimic the inherent complexity of non-linear physical systems in the real world. Considering the main biological interpretations of cellular signalling, in which complex behaviours and robust cellular responses emerge from the interaction of multiple pathways, we introduce two ASN representations: a stand-alone ASN and a coupled ASN. In particular we note how sophisticated cellular communication mechanisms can lead to effective controllers, where complicated problems can be divided into smaller and independent tasks.

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### 1. Introduction

Cellular signalling needs to engage in many forms of communication to enable cells to sense and respond to the outside world. This capability is vital for cells to survive and adapt to constantly fluctuating environments. In multicellular organisms, the role of cellular signalling is especially significant as it is responsible for the coordination of complex multicellular interactions and the production of collective responses.

Broadly speaking, cellular signalling is a sequence of events triggered by a biochemical signal that requires a cellular response. Signalling pathways are the simplest cellular structures connecting the outside environment with the genes they regulate. A closer inspection reveals that cellular signalling starts when a surface receptor binds an extracellular messenger, which diffuses an intracellular signal to an effector protein inside the cell. This then produces secondary messengers, which transmit the information further into the cell along signalling pathways. Spatially or temporally variable catalytic reactions or cascades of protein kinases lead to changes in gene expression, bringing about a change in cellular activity. Cells also show a complex internal organisation, which regulates the number of cellular components activated by

secondary messengers and guides the interactions between cellular regions. Crosstalk (Schwartz and Baron, 1999) captures the interaction between signalling pathways that leading to the formation of complex networks that produce a coordinated response.

In this paper, we extend our previous work on artificial signalling networks (ASNs) (Fuente et al., 2012) and suggest the use of crosstalk as a mechanism to model the structural and temporal topologies of cellular signalling, capturing its intrinsic dynamics. In order to test our model, we apply it to the control of a numerical dynamical system, whose properties mirror the complexity of the cellular environment.

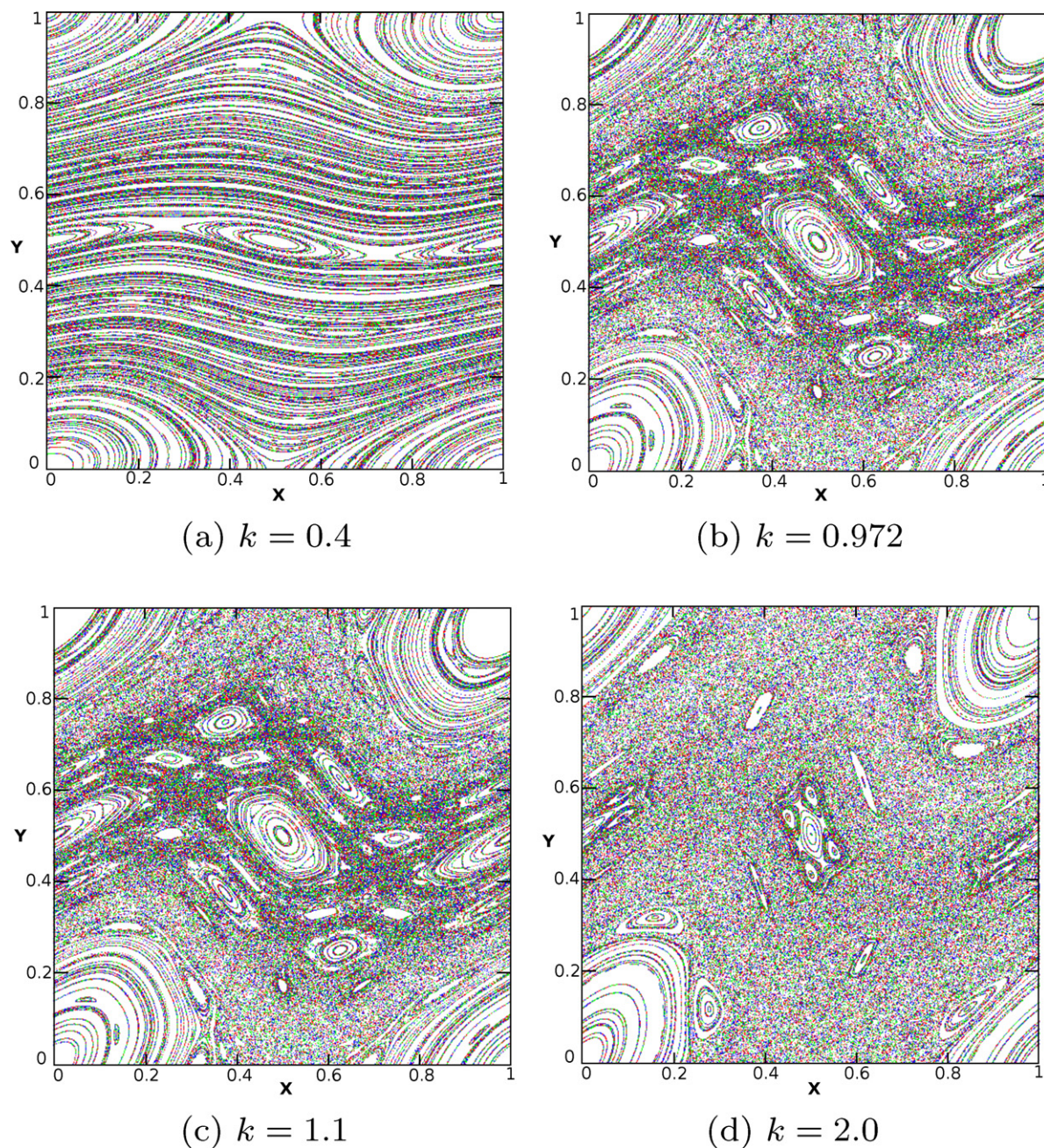
This paper is organised as follows: Section 2 presents a brief overview of dynamical systems, Section 3 reviews the modelling of ASNs, highlighting the challenges this involves, Section 4 presents the new model and proposes the evolutionary algorithm used to induce model instances, Section 5 presents results and analysis and Section 6 concludes the paper.

### 2. Dynamical systems

A dynamical system is a mathematical model consisting of a state space and a function, or *evolution rule*, that specifies its current state within the space state based on an initial condition (Stepney, 2011). The evolution rule defines the motion and behaviour of the system across the state space. Dynamical systems can be *autonomous* or *non-autonomous*. The former is a closed system whose dynamics are not perturbed by the outside world. The latter defines an open system changing over time, as inputs are received from an external environment. Likewise, dynamical

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**Fig. 1.** Sampled trajectories of Chirikov's standard map using different values of  $k$ , showing the transition from the ordered to the chaotic state. Each map is plotted using 400 randomly chosen initial points across the unit interval over 800 iterations.

systems can be *discrete* or *continuous* in time, depending on the type of evolution rule: difference equations in the former and differential equations in the latter.

Given a set of initial points within a discrete state space, the evolution rule defines their *trajectories* as a sequence of states over a period of time. A dynamical system where trajectories do not contract to a limited region of the state space is known as a *conservative* system.

Dynamical systems can display a wide range of behaviours. The most interesting are those involving holistic irregular and unpredictable properties; this atypical dynamism is known as *chaos*. Despite being deterministic, chaotic systems display aperiodic behaviours characterised by an exponential sensitivity to initial conditions and the existence of strange attractors. Whereas the former suggests that small changes in the initial conditions

convey highly different trajectories throughout the state space, the latter defines fractal and non-linear regions where trajectories may converge.

### 2.1. Chirikov's standard map

Chirikov's standard map (Chirikov, 1962) is a conservative and discrete two-dimensional dynamical system representing iteratively the interactions of two canonical variables:

$$\begin{aligned} x_{n+1} &= (x_n + y_{n+1}) \bmod 1 \\ y_{n+1} &= y_n - \frac{k}{2\pi} \sin(2\pi x_n) \end{aligned} \quad (1)$$

One of the map's main properties is its capacity to represent different dynamics as its nonlinearly increases. Thus, low values of  $k$

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