EVOLVING ARTIFICIAL CELL SIGNALING NETWORKS

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GOAL OF WORK PRESENTED IN THIS POSTER

We are investigating the use of artificial Cell Signaling Networks to implement computation, signal processing and (or) control functionality. In the following sections we review a number of the research issues which this raises.

INTRODUCTION

• **Cell Signaling networks** (CSNs) are bio-chemical systems of interacting molecules in cells. Typically, these systems take as inputs chemical signals generated within the cell or communicated from outside. These trigger a cascade of chemical reactions that result in changes of the state of the cell and (or) generate some chemical output, such as prokaryotic chemotaxis or coordination of cellular division.

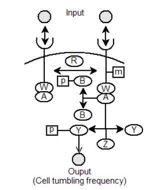

Figure 1: Schematic representation of bacterial chemotaxis signaling pathway, adapted from [1]. The output is designated by the tumbling frequency which is determined from the input, the concentration level of ligand bound to the membrane receptors. This signal transduction is carried out by the reaction cascade depicted by the proteins A, B, R, W, X and Z. Details on chemical reactions can be found in [1].

• CSNs can be regarded as special purpose computers [2]. In contrast to conventional silicon-based computers, the computation in CSNs is not realized by electronic circuits, but by **chemically reacting molecules** in the cell.

• **Realising** and **evolving** Artificial Cell Signaling Networks (ACSNs) may provide new ways to design computer systems for a variety of application areas.

• We are investigating the use of ACSNs to implement: **computation, signal processing** and (or) **control functionality.**

COMPUTATION

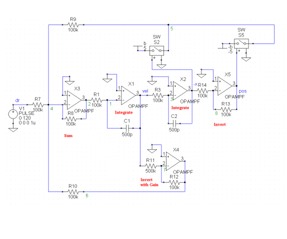

Figure 2: Schematic for the analog computer simulation of the driven constant-force magnitude oscilator.
http://physics.mercer.edu/petepag/yoyo.html

CSNs & ANALOG COMPUTERS

As a "computational" device, CSNs can be compared to analog computers:

• CSNs can be modelled with systems of continuous differential equations

• Analog computers are precisely designed to model the operation of a target dynamical system by creating an "analogous" system which shares the same dynamics

ADVANTAGES OF USING CSNs AS MOLECULAR ANALOG COMPUTERS

• CSNs may offer capabilities of **high speed** and small size that cannot be realised with solid state electronic technology.

• More critically, where it is required to interface computation with chemical interaction, a CSN may bypass difficult stages of signal transduction that would otherwise be required. This could have direct application in so-called **"smart drugs"** and other bio-medical interventions.

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EVOLUTION

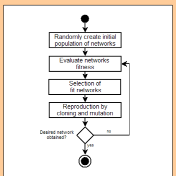

Figure 3: A: Flowchart of the Lakhesis evolutionary algorithm adapted from [5], the initial population of networks is randomly generated referring to genetic diversity. Fitness computation is obtained by: solving ODEs which allows one to compute steady states of the network, then the deviation of each node is calculated according to the mathematical computation we want the network to perform. Selection implies removal of unfit networks and reproduction correspond to asexual reproduction where mutation operators are applied. This process is repeated until we get a correct network performing the desired mathematical function.

One way to design ACNs to carry out computations is to use artificial **evolutionary techniques** [3, 4, 5]. Such techniques are relevant to the study of Artificial CSNs because:

• The complex, and unpredictable, interactions between different components of CSNs, make it very difficult to design them "by hand" to meet specific performance objectives.

• Natural evolution shows that in suitable circumstances, effective CSNs functionality can be achieved through evolutionary processes.

CROSSTALK

"Crosstalk" phenomena happen when signals from different pathways become mixed together, see Fig 4. In traditional communications and signal processing engineering, crosstalk is regarded as a **defect**. However, crosstalk in CSNs may also have potential **constructive** functionalities:

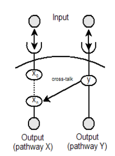

Figure 4: Schematic illustration of a CSN composed from two distinct cell signaling pathways with unique input and output, an interaction between pathways occurs as molecule y interacts with xn, this modulates the output ofpathway X.

• Adding uncorrelated "noise" to a functional signal may improve overall system behaviour. This is well known in conventional control systems engineering in the form of so-called "dither". Compare also, [6, 7] on constructive biological roles of noise.

• Crosstalk may provide a way of creating a large space of possible modifications / interactions between signaling pathways. Thus, although many cases of crosstalk may be immediately negative in their impact, crosstalk may still be a key mechanism in enabling **incremental evolutionary search** for more elaborate or complex cell signaling networks.`

ROBUSTNESS

• It is argued that key properties in biochemical networks are to be **robust**, this is so as to ensure their correct functioning [8].

• Alon et al. demonstrated from studying E. coli chemotaxis that molecular interactions can exhibit robustness [9, 10]. In this case it means that after a change in the stimulus concentration (input), the tumbling frequency (output) managed to reach a steady state that is equivalent to the pre-stimulus level.

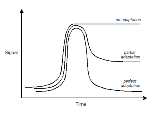

Figure 5: Representation of dynamic responses of a system to a stimuli taken from [13]. No adaptation is observedwhen the system response attains a new steady state following the change in input. Partial adaptation describe a partial recovery, the difference between the initial state and the new state is lower than the one observed in the previous case. Perfect adaptation is met when the system is able to come back to its initial state

FUTURE WORK

We want to address a number of questions:

• How to evolve systems of ACSNs that control each other?
• How to investigate the ability of those systems to create and sustain specific internal conditions (homeostasis)?
• How to investigate and quantify the robustness of such systems to external shocks and changes of conditions?
• How to transfer insights from this work to build more resilient "self-repairing" and adaptive control-systems?

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