CELLULAR DYNAMICAL SYSTEMS

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Abstract. This is an introduction to cellular dynamical systems theory, a mathematical strategy for creating dynamical models for the computer simulation of biological organs and membranes, and other systems exhibiting natural intelligence. Full details will be published elsewhere [1]. This strategy is based upon complex dynamics (an extension of nonlinear dynamical systems theory to networks of serially coupled dynamical systems) as described in earlier publications [2].

Historical introduction

Reaction/diffusion equations were introduced by the pioneers of biological morphogenesis: Fisher (1930), Kolmogorov-Petrovsky-Piscounov (1937), Rashevsky (1940), and Turing (1952). Rashevsky introduced spatial discretization corresponding to biological cells. These discretized reaction/diffusion systems are examples of cellular dynamical systems, probably the first in the literature. Further developments were made by Southwell (1940-45), Turing (1952), Thom (1966-1972) and Zeeman (1972-1977). The latter includes a heart model, and a simple brain model exhibiting short and long-term memory. The ideas outlined here are all inspired by these pioneers. For full bibliographies, see [1].

Cellular dynamical systems

By dynamical system we mean an autonomous system of coupled ordinary differential equations of the first order. More generally, we include vectorfields on manifolds, both finite and infinite dimensional, which we call state spaces. Thus, systems of coupled partial differential equations of evolution type are included, along with integro-differential-delay equations, and so on. By dynamical scheme we mean a dynamical system depending upon parameters in a supplementary manifold, the control space. Dynamical schemes may be serially coupled in various ways. The simplest, which suffices

for most of our applications, is called a static coupling. This is a function from the state space of one dynamical scheme to the control space of another. The canonical example is the driven pendulum. In this way, a finite set of dynamical schemes (nodes) may be serially coupled by an appropriate set of static couplings (directed edges) in a network (directed graph). This is the primary object of complex dynamical systems theory. Exemplary models for several physiological systems have been developed and run, producing convincing simulated data [2].

By cellular dynamical system we mean a complex dynamical system in which the nodes are all identical copies of a single dynamical scheme, the standard cell, and are associated with specific locations in a supplementary space, the physical substrate, or location space. Exemplary systems have been developed for reaction/diffusion systems by Southwell's relaxation method: discretization of the spatial variables. In these examples, pattern formation occurs by Turing bifurcation. One of the most-studied examples of this class is the Brussellator of Lefever and Prigogine. Other important examples of this construction are the heart and brain models of Zeeman. These models have something in common with the cellular automata of Von Neumann, yet possess more structure.

The behavior of a cellular dynamical system may be vizualized by Zeeman's projection method: an image of the location space (physical substrate) is projected into the response (bifurcation) diagram of the standard cell, where it moves about, clinging to the locus of attraction. Alternatively, the behavior may be vizualized by the graph method: attaching a seperate copy of the standard response diagram to each cell of the location space. Within this product space, the instantaneous state of the model may be represented by a graph, showing the attractor occupied by each cell, within its own response diagram.

In either case, the behavior of the complete cellular system may be tracked, as the controls of each cell are seperately manipulated, through an understanding of the standard response diagram provided by dynamical systems theory: attractors, basins, seperatrices, and their bifurcations. For an introduction to this subject, see [3].

Biological organ models

Organs typically contain many different types of cells.

In the unusual case that there were only one type of cell, one could imagine a model for the organ consisting of a single cellular dynamical system. This is the case with Zeeman's heart model. An explicit cellular dynamical model for the organ will require an explicit model for the standard cell, which (with luck) may be found in the specialized literature devoted to that cell.

However, if there are two distinct cells, then each will give rise to a distinct cellular dynamical model. The model for the organ will then consist of a coupled system of two cellular dynamical systems, one for each cell type. More generally, the organ model will consist of a complex dynamical system, comprising a network of distinct cellular dynamical models, one for each of the distinct cell types.

Moreover, even if there is only a single cell type in the organ (for example, a liver cell) a network of cellular models may nevertheless be required. For there are usually at least two important compartments in the organ: the intracellular space, and the extracellular space. The concentration of control metabolites or humoral substances (such as the pacemaker substance in Zeeman's heart model) in the extracellular space contributes a second cellular dynamical system to the model. This second system arises through the discretization of the nonlinear Fickian diffusion equation for the perfusion of metabolites through the organ. Even if the substance in the two compartments is the same (for example, cortisol in the adrenal cortex), there will be two distinct cellular systems in the organ model. The dynamics of the extracellular substance will usually be modeled by a (discretized) reaction/diffusion system, while the intracellular dynamics may be modeled by reaction kinetics alone.

Nonlinear spectroscopy

Even with enormous computers, the simulation of a detailed model of a realistic organ, on the scale of individual cells, will be too slow to be useful. Thus, for models which can interact fruitfully with researchers on the frontiers of science, we must use computational cells larger than a single cell. These computational cells will be assigned average values of the state variables of the individual biological cells (or subcellular units, or extracellular spaces) contained within it. If the size of the computational cell is varied through a sequence of increasing sizes, from a fraction of a single cell to the whole organ or organism, we obtain a family of distinct cellular dynamical

models for the same organ. Their spectrum of behaviors comprises the nonlinear spectral analysis of the modeling scheme used to construct the family of models. The shape of this spectrum may be very useful in optimizing a model for a specific purpose, as well as for understanding the physiology of the organ or target system.

Numerical methods and experiments

The destiny of a cellular dynamical model is a computer program. Although we may expect someday a theory of these models, it may not replace simulation as the dominant method of science, but only supplement it. Thus, we need a technology of numerical methods adapted to these large-scale simulations. Beyond brute-force integration of thousands of identical copies of the standard dynamical scheme with differing (and slowly changing) values of the control parameters, lookup-table methods might be employed for accelleration or economy. In any case, massively parallel hardware and software will be needed, along with new methods of monitoring large numbers of state variables. Color graphics is the method of choice at the moment, and we may imagine a color movie projected upon a model of the physical substrate of the organ as the monitoring scheme.

The current state of the art seems to be simple experiments with standard cells culled from the literature of the physical sciences, such as the Duffing pendulum, the cusp castrophe, and so on. From these experiments, we may try to recognize some functions of natural intelligence, such as memory, perception, decision, learning, and the like. A number of such experiments have been proposed elsewhere [3].

Bibliography

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