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Original Article

From Biophysics to Behavior
Catacomb2 and the Design of Biologically-Plausible Models for Spatial Navigation

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Abstract

A variety of approaches are available for using computational models to help understand neural processes over many levels of description, from sub-cellular processes to behavior. Alongside purely deductive bottom-up or top-down modeling, a systems design strategy has the advantage of providing a clear goal for the behavior of a complex model. The order in which biological details are added is dictated by functional requirements in terms of the tasks that the model should perform. Ideas from engineering can be mixed with those from biology to build systems in which some constituents are modeled in detail using biologically-realistic components, while others are implemented directly in software. This allows the areas of most interest to be studied within the context of a behaving system in which each component is constrained both by the biology it is intended to represent as well as the task it is required to perform within the system. The Catacomb2 modeling package has been developed to allow rapid and flexible design and study of complex multi-level systems ranging in scale from ion channels to whole animal behavior. The methodology, internal architecture, and capabilities of the system are described.

Its use is illustrated by a modeling case study in which hypotheses about how parahippocampal and hippocampal structures may be involved in spatial navigation tasks are implemented in a model of a virtual rat navigating through a virtual environment in search of a food reward. The model incorporates theta oscillations to separate encoding from retrieval and yields testable predictions about the phase relations of spiking activity to theta oscillations in different parts of the hippocampal formation at various stages of the behavioral task.

Index Entries: Computational neuroscience; simulation software; modeling; spatial navigation; hippocampus; theta rhythm.

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Introduction

Two tasks at which the capabilities of computers far exceed those of human researchers are the management of very large homogeneous volumes of data and the numerical calculation of the behavior of complex systems based on precise and complete formulations of their constituent parts.

Both of these capabilities are of great potential benefit to research in neuroscience, yet the uptake of database technology and the growth in the use of models has been much slower than in many other sciences. On one hand, this may be ascribed to the extreme heterogeneity of the information to be stored and processed, and on the other to the total absence of "precise and complete formulations" of the behavior of elementary constituents of neural systems. That is, heterogeneity is as much a problem in computing collective behavior as it is in storing and handling data. Indeed, ambitious recent developments such as CellML (www.cellml.org) or Neurospaces (Cornelis and De Schutter, 2003) intentionally blur the distinction between representations of the biological structure and of the mathematical properties of a system. They treat the mathematical formulation simply as more first-order information to be processed along with a system's logical and spatial structure, in order to derive higher level properties.

The impact of heterogeneity on the feasibility of modeling studies has often been underestimated, as characterized by the view that if we just work a little harder and make a bit more effort, then the methods that are so effective in, for example, theoretical physics, will yield equally fruitful and compelling results in neuroscience. This view neglects, or denies, a fundamental difference between physics and life sciences that Schroedinger (1956) describes as the difference between "hot" and "cold" systems. In a "hot" system (almost everything treated by theoretical physics) as you include more and more elementary units, their collective behavior begins to be independent of the detailed properties of the units themselves. Consequently, mathematical approximations get better and better for larger and larger systems. Cold systems (all living things) behave in the opposite manner, more analogous to a machine than to a statistical equilibrium, with the variety of realizable behaviors growing with increasing size.

A consequence of this is that although abstract mathematical models and detailed physics-style bottom-up models can both be useful, there is a whole domain of computational applications in neuroscience that is simply not represented in other scientific fields. These are the techniques appropriate to the study of complex "cold" systems in terms of information management and software engineering. They form a major constituent of the emergent field of neuroinformatics.

Because of the closer analogy of neural systems to machines (mechanical, computational or economic) than to perturbations of statistical equilibria, it is to be expected that much of the methodology and technology of neuroinformatics should owe more to engineering or commerce than to applied mathematics and theoretical physics. Thus, for example, the software systems of choice in computational neuroscience, as well as in the business community, include C^{++}, Java, and XML (Goddard et al., 2001a,b; Forss et al., 1999), whereas these systems have only achieved minimal penetration among physicists, presumably because they are not particularly useful for most research problems in physics. Likewise, neuroscience database technologies (Cannon et al., 2002) are more closely related to distributed shopping systems than to their highly centralized, astronomical counterparts (Wenger et al., 2000). One exception to the correspondence with business software is the extensive use of Lisp, the preferred language of artificial intelligence research, in the Surf-