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A GLOBAL MODEL OF NEURONAL COMMAND-CONTROL SYSTEMS *

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In learning of the death of Lars Onsager, friend and great scholar, it seemed appropriate to us, as a small tribute to his memory and his interests, to present some of our speculations regarding the organization of the nervous system. We hope that this essay may provide useful insights into such organization. We offer it in full awareness that it represents an oversimplification of the problem at hand and that its global extent is much too broad to be considered critical. We write it, nevertheless, because we consider that on certain occasions a use of metaphors about the intrinsic processes in a complex system may offer more to human discourse and understanding than the more precise but often cryptic language of the specialist.

A recent paper of ours (Iberall and Llinas, in press) presented a cybernetic view of command-control in complex living systems and offered some central ideas reached after a number of years of collaborative discourse. New advances in our biological and physical understanding, and further discussion, have led to the development of the following set of hypothetical theses for command-control in living systems, including memory. These theses are cast as a global model at the level of single cells. However, elaboration to the level of a brain, even a human brain, seems to us to be considerably simplified when the dynamic topology of the theses considered here are more fully explored, because we believe they offer a generalized approach to the problem of command-control.

(1) Motor and sensory properties in the nervous system originate from the same general cell substrate. This fundamental premise establishes the central (di) polar axis for motor-sensory performance of the organism (henceforth to be considered the cell).

(2) All brains are basically a progressive elaboration of ancient (primitive) cellular themes (Llinas, 1974). The command-control properties of multicellular organisms are veiwed as derived from the elaboration of themes already present in single cell forms, where one finds the essential polar principle of sensory and motor regulation clearly exhibited.

(3) The plasma membrane is a basic thermodynamic engine; its major functional characteristic is the control of admission characteristics of ions and other substrates to the cell. With the identification of molecular carrier structures and ionophores, it seems reasonable that the control of admission be exercised by the ionophore or carrier systems.

(4) The rolling of molecules at phase interfaces (a new hydrodynamic boundary condition for liquids) is the basis for low (electrical) energy control of membrane admission. The physical mechanism proposed is an electrical control of the bulk viscosity.

Bulk viscosity is essentially a physical measure of nonequipartitioned energy-time delays, here to be found as macromolecular channels in membranes. It is the ease of these molecules to serve as powered electrical

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* Invited paper. Dedicated to the memory of Lars Onsager.

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gatekeepers, to "recognize" the chemical form or control the chemical fate of passerby rolling molecules via nonholonomic constraint, that details the time delay mechanism. Form (a resistance to stress) is derived as the ratio of bulk to shear viscosity (λ/μ) (Iberall, 1975). Physically the stress tensor decomposes into undirected pressure, a rotation creating shear stress (momentum exchange from neighboring regions) and dilatational stresses which disappear into the internal structure. In a gel-like state, the apparent trivial process of volume dilatation becomes the all-significant process of switched action modes (conformational changes). A basic characteristic of a gel is that its state may be switched from solid to liquid electrically (conformational change due to charge redistribution) and that it derives its nature from a chemical skein which can polymerize water. These properties give the gel system the possibility of an electric command-control of the λ/μ ratio. Thus, the cell has an on-board engine for wide-band control of the λ/μ ratio, i.e. its gating form.

(5) The "cytoskeletal" system is a two-way conduit system which can provide communication between the membrane and the internal workshop of the cell and thus serves to regulate membrane admission characteristics (via a controlled bulk viscosity). A missing ingredient, the impediment to effective internal control of ionophoric admission, is the remoteness of the internal mechanisms of the cell. The internal factory processes have been depicted in current literature as a series of "workshops" within the cellular gel structures (Palade, 1975) (e.g., at organelles in Golgi apparatus, endoplasmic reticulum, and other membrane-bounded structures) wherein their competence to display factory form and function were related to the relatively slow diffusive response of the locally viscous gel as slow hydrodynamic processes. (A typical example of a local process might be the assembly of a protein which is created by many steps of chemical synthesis. While individual steps could be quite fast (e.g., 10^{-6} seconds) and also locally rate-governed within the local process plant by rolling boundary conditions, the great number of steps in synthesis would make the overall processes quite slow.) But then the real significance of the cytoskeletal system (microtubules, microfilaments and their related structures (Stephens and Edds, 1976; Wuerker and Kirkpatrick, 1972)); as an intracellular conduit system becomes apparent. While "internal fluid conduital systems" (pipes) would pose difficulties for fluidity control, facing the same limiting slowness of diffusion, an "external fluid conduit" (wires) which could be gated by surface molecular conformations, such as postulated in the sliding filament theory of muscle contraction (Huxley, 1969), would be an elegant solution for intracellular transport.

(6) The sensory mechanisms form a crasis in location and complexity with the motor system. According to this view, the membrane engine is the recipient of "sensory" flow from the external milieu directly or through an interposing set of cellular circuits. As far as the single cell goes, the simple solution of using the cytoskeleton for a two-way conduction system immediately makes itself evident. It transduces information via the membrane by field mechanical processes (e.g. electromagnetic, acoustic, electrochemical) into the system, and information by field and ~~matter~~ mechanics out to the membrane. Both motor and sensory functions are thus served by the same processes in the same circular chain.

(7) The membrane partakes in the direction of information flow in a synchronic oscillation mode; it alternates between in and out. An apt metaphor to describe the process within the membrane is yin-yang, the two-way transmission system within the cell, as stated above, being the microtubule—microfilament system. This notion is proposed following discoveries such as those of Lazaridis, which suggest that the perinuclear region is connected by a system of actin filaments to the plasma membrane (Lazarides, 1976). The stage is thus set for the total

regulation of all processes by the membrane engine.

This system may provide a regulation in which not only the genetic program can be expressed, by connection between nucleus, functional factory organelles and the membrane but, also, the membrane's admission control is in the chain to implement command-control which no longer becomes a "thing", but the process itself.

And so conversely the membrane engine sits as the mediator between outside and inside and controls the loading dock and what it lets in or out.

Expressed by the yin-yang metaphor, consider outside informative matter-energy as *A* and inside informative matter-energy as *B*. The active membrane looks outward and gets a signal from outside. It turns inward and gets a signal from therein. It is thus constantly being confronted by a double bind (*A* and *B*). And its problem is to resolve these conflicts moment by moment by introducing or rearranging new membrane components or changing the functional state of these components and thus using its admission control characteristics.

(8) The ionophoric or transport admission characteristic itself carries the memory. And where is memory? As the internal factories making various ingredients are cued from both membrane and nucleus, one of them — the protein factory — controls the kind of message it inscribes within these catalytic soon-to-be globular proteins (Spiegelman, see for example Mills et al., 1973). When these are elaborated and protrude through the membrane to become mosaic proteins, they carry the memory.

(9) The outside world may not easily write on the internal nucleus. "Where is fancy bred — in the heart or in the head?" - one of the primitive questions that Warren McCulloch asked. Where is the geist of the system? Is it "heredity" or "environment" that determines the system? Not all of the system's characteristics are writ on the nucleus or by the nucleus into the membrane.

What does the outside environment do? — It provides the nucleus with information (via the membrane) to "remind" it when and what part of its message to express. It is Cartesian writ (by chemical clockwork engines) but not hard-wired and hard-geared. The coupling is reliable and persistent, but softly spoken (gene expression). It must be adaptive to the milieu, but in a sheltered fashion.

Those who will philosophically attune themselves to these theses will recognize them as Plato's shadows in the cave, a most exciting realization by two individuals who would never have selected that Platonic image as their starting point. Remarkably, it is the nucleus who only "sees" the shadows of reality, who puts forth its stored genetic memory and a newly minted epigenetic memory into its outer membrane structure. It writes that distorted view of reality, and yet it permits "outside reality" to additionally key and distort that reality (flickering shadows in the cave). Most remarkably, that system is good enough to be adaptive and survive and persist reliably for billions of years.

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