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Final Report

Title: Autonomous Agents: The Origins and Co-evolution of Reproducing Molecular Systems, NAG 2-1091

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The central aim of this award concerned an investigation into, and adequate formulation of, the concept of an "autonomous agent." If we consider a bacterium swimming upstream in a glucose gradient, we are willing to say of the bacterium that it is going to get food. That is, we are willing, and do, describe the bacterium as acting on its own behalf in an environment. All free living cells are, in this sense, autonomous agents. But the bacterium is "just" a set of molecules. We define an autonomous agent as a physical system able to act on its own behalf in an environment, then ask, "What must a physical system be to be an autonomous agent?"

My tentative definition for a molecular autonomous agent is that it must be self-reproducing and carry out at least one thermodynamic work cycle.

The work carried out in this grant involved, among other features, the development of a detailed model of a molecular autonomous agent, and study of the kinetics of this system. In particular, a molecular autonomous agent must, by the above tentative definition, not only reproduce, but must carry out at least one work cycle. I took, as a simple example of a self-reproducing molecular system, the single-stranded DNA hexamer 3'CCGCGG5' which can line up and ligate its two complementary trimers, 5'CCG3' and 5'CGG3'. But the two ligated trimers constitute the same molecular sequence in the 3' to 5' direction as the initial hexamer, hence this system is autocatalytic.

On the other hand, the above system is not yet an autonomous agent, for the reaction couple is purely exergonic. To create a first hypothetical autonomous agent, I linked to further hypothetical reaction couples to the trimer hexamer system, namely, a pyrophosphate to phosphate reaction whose large free energy drop, coupled to the synthesis of hexamer, drives endergonic, hence excess, synthesis of the DNA hexamer. This excess synthesis means that the system replicates better in the presence of the pyrophosophate-phosphate couple than without it. Then, to restore the initial pyrophosophate concentration, I invoked a hypothetical reaction in which a photon activates an electron to an excited state which couples to resynthesis of the pyrophosophate from the monophosphates, and the electron gives up the energy of its excited state.

Overall the autonomous agent is an open thermodynamic system whose "food" consists in two DNA trimers and the photon source. The work cycle, linking exergonic and endergònic reactions, is apparent in the net rotation of pyrophosophate to monophosphate back to pyrophospate. Indeed, under some parameter values, this system shows a temporal limit cycle as well.

At the minimum, autonomous agents, as I have defined them, are a new class of chemical reaction network. At a maximum, they may constitute a proper definition of life itself.

In the simulation work under the grant, carried out in collaboration with biophysicist Peter Wills and several students at the Santa Fe Institute and in New Zealand, we modeled the autonomous agent in terms of the appropriate differential equations for the reaction system described above. The resulting system has thirteen kinetic parameters. We undertook an exploration of this parameter space to define the conditions under which the autonomous agent, necessarily a non-equilibrium system, reproduced most efficiently. We found, therefore, in the thirteen parameter space, a fitness landscape, determined that landscape was multipeaked and correlated, and most importantly, confirmed that the autonomous agent out reproduces a mere DNA hexamer trimer system. Thus, natural selection would select for the autonomous agent.

In additional work, I carried out an analysis of the novel concepts involved in this new class of reaction networks, including a critique of the concept of a work cycle itself, a new analysis of the concept of work as the organized release of energy, the analysis of two types of closure in an autonomous agent, first, a catalytic closure such that all reactions that must be catalyzed are catalyzed, and second, a work task closure by which an autonomous agent literally constructs a rough second copy of itself via the linking of exergonic and endergonic reactions.

Further work elucidated the evolutionary properties of autonomous agents, including evolution by what Darwin called preadaptations. Here a causal consequence of part of an organism which had no functional use comes to be useful in a new environment, hence is subjected to natural selection. The core issue is whether it is possible to finitely prestate all possible exaptations. I believe the answer is "No," and that this failure means that we cannot prestate the configuration space of a biosphere. But, in turn, this suggests a radical shift in how we do science, for in the familiar cases, such as the statistical mechanics of a large number, N, of gas particles in a liter box, we can finitely prestate all possible positions and mementa in a 6N dimensional phase space. This issue was also explored.

Further work determined that autonomous agents persistently invade a chemical, morphological, and behaviorial "adjacent possible" in which, at levels of complexity above simple atoms, the universe is non-ergodic on vastly long time scales compared to the current history of the universe. Hence the Darwinian preadaptations that come into existence change the history of the physical universe. In turn, this probably implies that the incapacity to finitely prestate the configuration space of a biosphere means that we cannot deduce the unfolding of the universe, not only because of the quantum chance, but because we cannot prestate the relevant macroscopic classical features of a biosphere that will matter in its persistent evolution.

This grant from NASA has been used to study a central object in Astrobiology, autonomous agents. The results are now in final draft form as a book for Oxford University Press, to be published spring 2000. It is my belief that autonomous agents will be central to the "general biology" that Astrobiology strives to become.