Meetings

Hierarchical Structures

Everyone is aware of significant groupings of things—in taxonomy, in biological structures, in social structures, and in material objects from crystals to stellar systems. An interesting aspect is how the characteristics of a group are related to the nature of the parts and to the characteristics of other groupings—the properties of order and disorder. Applications of these ideas in biology, crystallography, cosmology, and philosophy were discussed by some 50 scientists, each an expert in one of five or six different disciplines, at a symposium organized by Albert G. Wilson (astronomer), Ralph W. Gerard (biologist), Lancelot L. Whyte (historian), and Donna Wilson (sociologist, who prepared a bibliographical outline circulated in advance). The symposium was held at the Douglas Advanced Research Laboratories, Huntington Beach, California (18–20 November 1968).

The term "hierarchy" was first applied to social and religious organizations in which the relation between groups was one of control or dominance. Mario Bunge (philosopher, McGill University) stressed the importance of asymmetric relations between levels, the members of each level being "bosses" of the next lower level. However, in the history traced by L. L. Whyte and C. D. Leake (University of California Medical Center, San Francisco), it was clear that Aristotle and Theophrastus applied hierarchical structures to the taxonomy of animals and plants, where a species member cannot be said to boss or control a subspecies.

Even more obviously, the fundamental particles in the lowest level of Harlow Shapley's hierarchy of material systems [*Of Stars and Men* (Beacon Press, Boston, 1958)] are not bossed by the atoms, molecules, cells, men, and galaxies in levels above them. In fact, this type of materials hierarchy some think may arise in the mind of man—a psychological result of our upbringing that makes it easier for us to conceive of things arranged in branching, pyramidal hierarchies. The French philosopher Ramus wrote in 1550 that "everything is formed of little units, and the mind groups these." Alternatively, the ranking of levels, and their relations in a hierarchy, may reflect the process of formation, as in Darwin's evolution of biological species.

Of course, it is necessary to have discrete units to form a hierarchy; continuous fields or smooth distributions will not suffice. Cyril S. Smith (metallurgist, M.I.T.) described the history of understanding metals as aggregates of crystals, magnetic domains, and impurities. Generally, imperfections form the unit boundaries in pure substances, and interaction energies often impose a regular pattern on these boundaries (which have been extensively studied in soap-bubble froth and by mathematical models of space-filling polyhedra). Many patterns have emerged, corresponding to various forms of equilibrium, and Smith feels that artists, rather than scientists, may be better able to study these patterns.

Digital computers handle discrete inputs and outputs in large quantity. F. E. Tonge (mathematician, University of California, Irvine) noted that the use of subroutines makes computer programming hierarchical, but that this is for the convenience of human programmers rather than the machines, which are linear processors and must be specially coded for subroutines. R. W. Lucky (Bell Laboratories) reported efforts to produce error-free codes (for the transmission of information) by "concatination," or codes within codes, that form a system similar to a hierarchy, and may bear on the DNA genetic codes of interest to the microbiologist, or the operation of brain and nervous system.

Leake stressed the structural hierarchies of biology, based on the cell theory dating back to 1839. Cells of various types form the organs in a human body and all other living organisms except viruses. These structures, probably the result of evolution, are organized by principles of purpose and process, replacing the dominance or "bossism" in social hierarchies. In one organism, such principles seem to control the organs and processes at all levels, revealing an elaborate network of influence based on the chemical action of enzymes from the interior, and of other chemical agents from the environment. In fact, the environs set up a whole new hierarchy—the topic of ecological studies.

H. H. Pattee (biophysicist, Stanford University) spoke about the chemical hierarchy within living cells, contrasting statistical models and detailed physical theory whereby characteristics of atoms should control their groupings in proteins and DNA. It is clear that these aggregates control details of growth. Just why the relatively few forms of polymers are preferred from the billions of billions of possible forms cannot be rigorously explained by detailed physical theory of the strengths of chemical bonds. Robert Rosen (biochemist, State University of New York at Buffalo) feels that the organizational principles within cells may be derived from a kind of chemical statistical mechanics, but this will not be possible until we discover some new subcellular observables comparable to the perfect gas laws in ordinary statistical mechanics. Both Rosen and Pattee pointed to the very complex molecular growth patterns simulated by a sequence generator that adds units on the front, right, or left of a structure, according to simple rules.

Turning to cosmology, where "purpose" is not assumed, nowadays, E. R. Harrison (astrophysicist, University of Massachusetts) noted that the laws of physics appear adequate to handle the various levels of the hierarchy from atoms to galaxies. The frontiers of physics where there are strong disagreements lie principally in the realms of the very small (fundamental particles) and the very large (cosmology). We are well aware of the discrete nature of atoms, stars, and galaxies, but cosmologists treat the material of the universe as if it were a uniform fluid. From gravitational theory and zero cosmological constant, we get models in which matter is very hot and highly compressed 10^{10} years ago. (The initial "big bang" at that time seems to have been confirmed by recent observations of the 3°K background of radio waves.)

Harrison raised the basic question: How did the presently observed hierarchical structure of planets, stars, and galaxies arise from a fluid that was originally compressed to extreme density? Jeans's idea was that the expanding fluid would be gravitationally unstable, so that small, chance excesses of density would grow. However, the billion-degree temperature during early stages allows no density excesses that can grow to the size of a galaxy in 10^{10} years. More recently, Novikov suggested "lagging cores" to explain quasars but these have too short a lifetime to explain the far more numerous galaxies. Efforts to use matter and antimatter appear quite promising, but Harrison stressed that until we have a satisfactory cosmogony, capable of explaining the origin of galaxies and their salient features, we shall not be able to understand why structure on the smaller scale exists.

Michele Kaufman (astrophysicist, Brown University) reported her calculations of galaxy formation by electrostatic forces, assuming (with D. Layzer of Harvard) that the early stages were not so hot. (The present 3°K background must then be explained as the remains of intense stellar radiation scattered by interstellar dust about 10^8 years after creation.) She predicts a hierarchy of density concentrations about 1000 seconds after creation, and shows that they would form objects the size of star clusters and galaxies today.

Some details of the regularity we see in the universe today among nonorganic objects were summarized by Albert G. Wilson (astronomer, Douglas Advanced Research Laboratories) who sees a hierarchy of interacting "modules" or groupings. The interactions are different at different levels, which range from atomic size up through meteorites, planets, stars, star clusters, galaxies, and clusters of galaxies to clusters of clusters. Interactions are roughly symmetrical between members of one level (horizontal interactions), but highly unsymmetrical between members of different levels (vertical interactions). The structure at different levels is probably associated with the nature of space and time at each level, an extension of Leibnitz's views of structure and space.

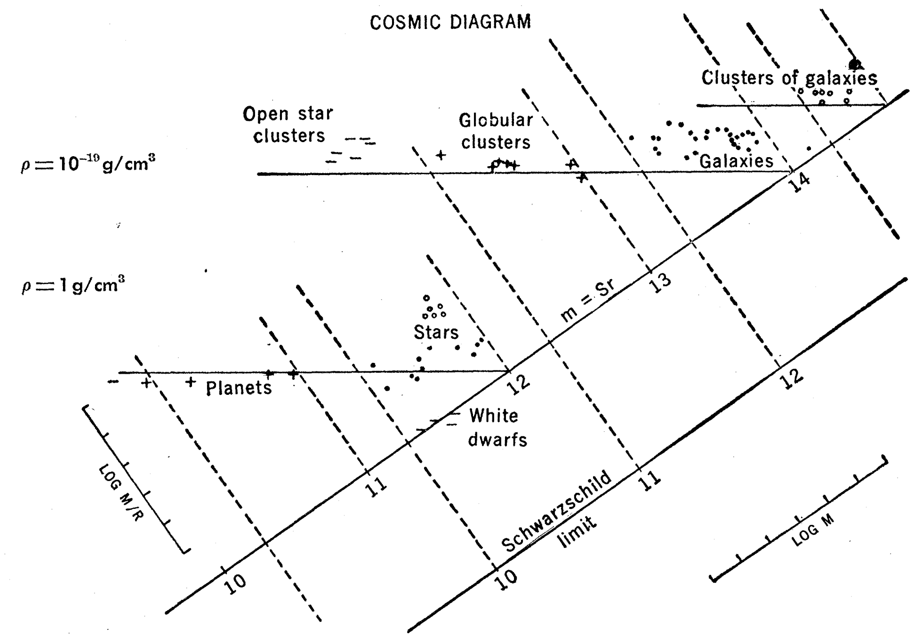

Fig. 1. Wilson's relations between masses and radii of celestial objects. The axes, log m (in grams) versus log m/r (in g/cm) are tilted at 45 degrees. One heavy line shows the limit, $m/r = S = 10^{39.4}$, and the other shows the Schwarzschild limit, $m/r = c^2/2G$. The numbers along these lines are powers of $S^{1/8}$ used by Wilson as frequencies characteristic of the various types of objects.

At the atomic level there are three dimensionless constants of possible significance: a quantity defined by Hopf, $S = e^2/Gm_pm_e = 10^{39.4}$, Sommerfeld's fine-structure constant, $\alpha = 2\pi e^2/hc = 1/137.03767$ (recently found from quasar spectra to have remained constant for at least 2 billion years), and the proton-electron mass ratio, $m_p/m_e = 1836.12$. Note that $8\pi^2 S = 2^{1/\alpha}$. At the galaxy level, astronomers have determined the expansion parameter (Hubble constant), $H = 100$ km sec^{-1} Mpc^{-1} $= 1/10^{10}$ years (age of the universe), and the present mean density of the universe, $\rho = 10^{-30}$ g/cm^3. Eddington noted that the radius of the universe, $R = c/H$, is such that its ratio to the Bohr orbit (size of the hydrogen atom) $a_0 = h^2/4\pi^2 m_e e^2$, is $R/a_0 = S$, and that the mass ratio, $\bar{\rho}R^3/m_p = S^2$, where $\bar{\rho}R^3 = M$ is about one-fourth the mass of the visible universe.

Admitting that this analysis is close to numerology, Wilson infers that modules in the universal hierarchy should be characterized by mass (m) and radius (r), both well known for atomic particles, planets, and stars, and fairly well known for galaxies and clusters of galaxies. He reports additional "vertical relations" between atomic and cosmic quantities. Over the ranges r/a_0 (from 1 to S) and m/m_p (from 1 to S^2) cosmic bodies are limited in m/r to about 3×10^{24} g/cm. On the plot of log m/r versus log m shown in Fig. 1, Wilson finds that the moon, planets, and stars fall close to one line of slope 2/3, which corresponds to densities of the order of 1 g/cm^3. Star clusters and galaxies fall close to a parallel line corresponding to densities near 10^{-19} g/cm^3, and clusters fall close to a third line corresponding to densities near 10^{-29} g/cm^3. All three lines terminate at log $m/r = 23.3$ (in g/cm), or at $m = Sr$. Wilson has had some success in predicting bounds on the masses of planets, stars, globular clusters, galaxies, and clusters of galaxies from a series of powers of S corresponding to overtones of frequencies characterizing each of the modules.

It was generally agreed by the conferees that little progress has been made in understanding the nature of hierarchies and the possible relations between groups of discrete entities. It would be important to find relations that can be transferred from one set to another, although there is the danger that some sets are not homologous with others (for example, biological versus inorganic, or upward-growing versus downward-growing). Undoubtedly, the interactions between entities account for the emergence of significant modules, or levels, or wholes which have properties other than expected from their components. One of the difficulties is that several different hierarchies can often be found in the same set of entities. When the levels are lasting, they would seem to be formed of stable structures, but Rosen thinks that biological levels are centered on unstable equilibria.

The proceedings of the symposium will be published in book form, and will hopefully stimulate further discussion of the fascinating problems of order and disorder.

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Immunology of Mouse Mammary Tumor Virus

Several different antigenic components have been found in the virion of the mouse mammary tumor virus (MTV). The MTV antigens fall into two classes: whole virion or coat antigens and soluble antigens. They can be demonstrated by the induction of specific antibodies in rabbits; also, mice proved to be capable of producing antibodies to some of these antigens. These new findings were brought out in a working conference on "Immunology of Mouse Mammary Tumors" held at the Institute for Medical Research, Camden, New Jersey, 11–13 November 1968.

The virion as a whole or a large subunit thereof seems to be capable of inducing precipitating serum antibodies in rabbits and agent-free mice. This reaction was reported by Phyllis Blair (University of California, Berkeley) and was confirmed by several laboratories. Virus from all mouse strains tested by Blair demonstrated a common coat antigen. Robert Nowinski (Sloan Kettering Institute, New York) reported on antibodies to a soluble antigen which presumably is located in the interior of the particle; this fact, also, was confirmed by several other groups. Louis Sibal (National Cancer Institute) reported finding two antigens after treating virion preparations with Tween-ether. With the aid of immunofluorescence, Peter Bentvelzen and J. H. Daams (Netherlands Cancer Institute, Amsterdam) found an antigen thought to be an early protein of the virus, in hemopoetic organs and in the mammary gland of infected mice. In the GR strain of mice, in which the MTV cannot be eliminated by foster nursing, this antigen was found in all organs. Using both immunological methods and bioassays, these investigators demonstrated that MTV can be released after irradiation or treatment with urethane in mouse strains which were assumed to be without MTV.

The opening session of the conference was chaired by Werner Henle (University of Pennsylvania, Philadelphia) who discussed similarities and differences of MTV and the myxoviruses. These complex viruses, rich in lipids, have much in common.

Chemically induced premalignant tissues of the mammary gland, which have been serially transplanted for more than 4 years, proved to contain new antigens, which are not MTV-derived, in spite of the presence of the virus. In this work reported by Glenn Slemmer (Institute for Cancer Research, Philadelphia), no difference in antigenicity could be detected between these premalignant tissues and the tumors which arose in them. Transplants of the premalignant tissues used to immunize the animals frequently gave rise to normal outgrowths. This was probably due to selection of a normal cell population present from the beginning in the transplant. Obviously, these normal cells do not contain the new antigens.

MTV antibody production in mice was a major topic of the conference. For many years after the discovery of the milk agent, attempts to demonstrate antibodies in mice were unsuccessful. It was believed that MTV was nonantigenic in mice. Contrary to these earlier results, MTV antibodies in mice were reported from almost all laboratories. With the possible exception of the GR strain of mice, there is no true tolerance to MTV. In most cases the antibodies were to the whole virion, or a major component of it, because treatment of the antigen with ether resulted in loss of the immunodiffusion line. Blair, who first demonstrated precipitating MTV antibodies in mice, usually used a few small inoculations of impure preparations from mammary glands without adjuvant. She was able to demonstrate antibodies to what appeared to be the whole virion. Otto Plescia and M. Menon (Rutgers University) reported on the enhancement of antigenic reactions caused by coupling the MTV virion with a strong antigen, such as bovine serum albumin. The reports from the various laboratories emphasized the dependence on methodology for detection of antibodies in mice. Some procedures seemed to induce antibodies to the whole virion coat and still others to a soluble internal antigen, as well as the coat. Weekly intramuscular inoculations of a virus in complete Freund's adjuvant in adult C57BL male mice, followed by a final booster without adjuvant, and bleeding 3 to 4 days later, gave, even after ten inoculations, no discernible antibodies by immunodiffusion test according to Dan Moore and Jesse Charney (Institute for Medical Research, New Jersey). However, when cells from an induced tumor were grown intramuscularly in isologous agent-free, C57BL/Haag mice, a good antibody response was obtained when the absorbed mouse sera were tested against purified virions. However, if the virions were pretreated with ethyl ether, no precipitation line was observed, thus indicating that the antibodies were against the whole virion or one of its major ether-sensitive components.

In another immunizing procedure, male and female mice from several strains were given a single, intraperitoneal injection of purified virus in complete Freund's adjuvant. A small booster dose of virions was given 90 days later. (This procedure has been shown by Sibal *et al.* [*Proc. Soc. Exp. Biol. Med.* **127**, 726 (1968)] to be effective in producing good titer antiserum to Rauscher virus.) Seven days after the booster inoculation, all the sera contained antibodies. Females in all strains gave stronger immunodiffusion lines than their littermate males. Strains BALB/c and RIIIf gave stronger lines than did types Af and C57BL.

The effect of thymectomy was reported by Edmund Yunis (University of Minnesota). Thymectomizing neonatal mice of high cancer strain C3H caused a decrease in incidence and a delayed development of mammary tumors. The question of tolerance and tumor development was discussed at some length. It was hypothesized that MTV-associated antigens cause a breakdown in tolerance followed by (i) a virus-host cell interaction; (ii) damage associated with immune response; and (iii) development of malignancy. The way in which thymectomy delays and decreases tumor incidence may be in