maximum predator life-span is included, this will perhaps make the model discussed above unrealistic during that part of the limit cycle where the victim density is very low.

MICHAEL E. GILPIN
Department of Population and Environmental Biology, University of California, Irvine 92664

References and Notes

1. M. L. Rosenzweig, *Science* **171**, 385 (1971).
2. ——— and R. H. MacArthur, *Amer. Natur.* **97**, 209 (1963).
3. C. D. McAllister, R. J. LeBrasseur, T. R. Parsons, *Science* **175**, 562 (1972).
4. The calculations Rosenzweig carried out to obtain figure 2 in (*1*) are apparently in error. For $K = 200$, the prey population would be reduced to a value very close to zero during each cycle. The extinction of the prey (the extinction of the predators would soon follow) could very easily be the result of computer truncations.
5. M. E. Gilpin, in preparation.
6. T. V. Davies and E. M. James, *Nonlinear Differential Equations* (Addison-Wesley, Reading, Mass., 1966).
7. M. L. Rosenzweig, personal communication.
8. Research supported by PHS grant ES-00121-04.

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Most of what Gilpin says is quite right. Extinction in my simulation of model 4 *is* caused by a truncation; mathematically, model 4 does indeed reach a limit cycle. However, that truncation was designed into the system for the sake of biological reality; I maintain that it was proper to do that and proper to issue the warning based on it. The value of V at the low point of the cycle is just unrealistically small.

Riebesell (*1*) has undertaken simulations of a systematic series of two-species exploitative systems. He has included random environmental fluctuations. In general, he finds that the nontrivial equilibria of exploitative systems can be roughly sorted into four types. The first includes those in which the victim's equilibrium V (that is, $\hat{V}$) is so close to K that simulated uncertainty produces rapid predator extinction. The second includes those with slightly lower $\hat{V}$; they are steady states despite the randomness. The third type is a band of still smaller $\hat{V}$ values; these produce the limit cycles of Gilpin. The last type includes the smallest values of $\hat{V}$, values so low that their associated limit cycles are unrealistic; either or both species become extinct. Cases of this last type correspond to ones in which strong enrichment is simulated, because, as I showed in my report (*2*), an increase in K has the same effect on stability as a decrease in $\hat{V}$. Thus a totally realistic approach to the problem demands that one deal with the probability that enrichment can meaningfully increase extinction rates.

In addition to that, even a change from a steady state to an oscillation is worthy of the concern of resource managers. Oscillation would produce its own problems: among them are fluctuations in the food supply, fluctuations in the labor market, and the need for storage facilities to damp the effect of the oscillation on consumers.

In defense of MacArthur's and my original work (*3*), it should be stated that we noted the problem of global stability therein. The section devoted to it included several cases in which we deduced the existence of limit cycles. We also admitted that graphical theory was incomplete without a clear understanding of global stability.

I should add that Gilpin's proof of limit cycles is unconvincing. It depends on the assumption that, in order to reach extinction, a population must ride a vector which intersects an axis. That is not so. The vector might reach a confluence with the axis—merge with it without crossing it.

May (*4*) has developed a convincing argument for the generality of limit cycles. Therefore, Gilpin's conclusion is perfectly accurate.

M. L. ROSENZWEIG
Department of Biology, University of New Mexico, Albuquerque 87106

References and Notes

1. J. Riebesell, thesis, State University of New York at Albany (1971).
2. M. L. Rosenzweig, *Science* **171**, 385 (1971).
3. ——— and R. H. MacArthur, *Amer. Natur.* **97**, 209 (1963).
4. R. May, *Science* **177**, 900 (1972). By coincidence, both May and Gilpin sent me copies of their manuscripts within a period of several days during the winter of 1971–72. They clearly have arrived at the same conclusions independently of each other and of Riebesell.

19 June 1972

Meetings

Immunology and Genetics

Thirty West Coast geneticists met with specialists in various fields of immunology at La Jolla, California, 25–26 February, to explore research and clinical aspects of the interface of immunology and genetics. The workshop-symposium was supported by the National Genetics Foundation.

Genetic control of immune responsiveness to specific antigens and the possible relation of such control to histocompatibility systems of mice, guinea pigs, and man were considered first. The antibody response involves a complicated interaction between thymus-derived antigen-reactive lymphocytes (T cells) and bone marrow–derived, antibody-producing cell precursors (B cells). A T cell capable of recognizing the specific immunogen seems to stimulate proliferation of and specific antibody production by B cells. Immune response (Ir) genes and antigen recognition were discussed by H. O. McDevitt (Stanford) and B. Benacerraf (Harvard). For some Ir genes, both responder (R) and nonresponder (NR) strains of mice and guinea pigs give a primary 19*S* response, but only R strains give a 7*S* secondary response. T cells appear to respond to "carrier" determinants on a given antigen, while the structure of the antibody combining site (idiotype) is a function of the structural genes for the immunoglobulins and is expressed in B cells. Genetic loci controlling graft rejection and amount of antibody produced and affecting antibody specificity map in a region of mouse linkage group IX. Ir maps between H-2^K and H-2^D, the two well-separated cistrons of the major histocompatibility system in the mouse (homologous with the LA and Four cistrons in the human HL-A system). Ir seems to comprise a set of several or many linked genes with dif-

fering specificity, possibly evolved originally for other cell surface functions. These genes appear to be distinct from the array of structural genes required to account for the diversity of amino acid sequences in the variable regions of immunoglobulins.

M. Cohn and M. Weigert (Salk Institute) used lambda myeloma proteins with antibody specificity to dextran and kappa myeloma proteins with antibody specificity to pneumococcal C carbohydrate (phosphorylcholine) as antigens to elicit isoantibodies against antibody combining sites (antibody to idiotype) in mice. Ability to produce a particular idiotype in various strains appears to be associated with a particular immunoglobulin heavy chain allotype, but not with any particular H-2 phenotype.

Inherited defects of cellular and humoral immunity in man provide counterparts to the experimental manipulation of immune systems in animals. H. H. Fudenberg (University of California, San Francisco) reviewed deficiency syndromes affecting stem cells, B cells, and T cells. The clinical severity varies, according to the particular class of cells and immunoglobulins affected. Inherited syndromes of neutrophil and complement dysfunction and autoimmune disorders also may be responsible for impaired host defenses. Although many of these syndromes are determined by single autosomal or X-linked genes, there are still no clues to the normal functions of such genes in the development and maintenance of immune responsiveness. Methods are too insensitive to distinguish whether there is a normal number of cells with decreased synthetic capacity or a decreased number of cells with normal synthetic capacity, or some block in the secretion of synthesized immunoglobulins in the antibody-deficiency conditions.

E. R. Giblett (University of Washington, Seattle) summarized definitive work by others on the genetic and enzymatic control of ABO and Lewis specificities on human red blood cell membranes and on blood group substances in body secretions, such as colostrum, ovarian cyst fluid, and saliva. The gene products are transferases which successively add specific sugar moieties to the carbohydrate chains attached through serine or threonine residues to a peptide backbone. The Lewis specificity has been found on sphingolipids in plasma and tumor tissue, as well as on glycoproteins. The distinction between A_1 and A_2 reactivity in the ABO system has been partially clarified with transferase enzyme assays. Results indicate that these two phenotypes differ in the density of receptor molecules per cell. Such steric relationships of antigenic groups on membranes are also a crucial issue in current studies of histocompatibility antigens.

P. Terasaki (University of California, Los Angeles) reviewed multiple aspects of human transplantation genetics. The two cistrons of the major histocompatibility system have many alleles. Although recombination occurs at about 1 percent frequency between the two cistrons, haplotypes representing specific *cis* pairs of alleles at the two loci are maintained in linkage disequilibrium, either because of steric requirements of the structure of histocompatibility antigens or because of some unknown selective forces. There are marked racial and ethnic differences in allele and haplotype frequencies. Extensive data with kidney transplants confirm the importance of the best possible "match" of donor and recipient. However, surviving mismatched transplants occur—either because of effective immunosuppressive therapy or, more interestingly, because of cross-reactivity between certain HL-A antigens. With a method in which platelet absorption was used before testing cytotoxicity, there were no cross-reactions between the LA and Four series, but a varying degree of cross-reactivity between specific pairs within each series. Recipient responsiveness has been examined in patients who have had a second transplantation, with testing for the presence of preformed cytotoxins before the second transplant. Those lacking such cytotoxins had much better survival. Similarly, half of hemodialysis patients do not develop cytotoxic antibody from transfusions and have better survival than those who are sensitized. Whether responsiveness in this context is homologous with the immune response genes discussed above in animal systems is simply unknown. It is known, however, that one-third of Rh-negative volunteers immunized with Rh-positive cells fail to respond with antibody to Rh.

HL-A phenotype frequencies have been determined for a great many diseases in a search for some meaningful associations between disease susceptibility or disease resistance and the HL-A system. Several reports have shown an excess of individuals with HL-A5 phenotype among patients with Hodgkin's disease having long survival. Leukemias, many varieties of cancer, rheumatoid arthritis, lupus erythematosus, psoriasis, and multiple sclerosis have been studied, with interesting new leads for the last three diseases. Such associations could represent the function of certain HL-A antigens on cell surfaces as virus receptors or the effect of HL-A linked Ir genes or other linked genes. However, any statistical associations must be viewed with caution. At least 25 specificities are compared (P value must be lower than .002 to suggest biological significance), and the ethnic variation in phenotype frequencies makes matching of control groups difficult.

R. A. Reisfeld (Scripps, La Jolla) presented chemical data on the nature of the histocompatibility antigens. Antigenic reactivity is retained even when most of the carbohydrate has been removed enzymatically, but protein denaturants destroy antigenicity. Comparisons of peptide maps and amino acid composition suggest that antigenic differences may be due to differences in amino acid sequences. The microheterogeneity found with immunoglobulins appears to be absent; for example, only the 24 tryptic peptides expected from a composition of 18 lysyl and 5 arginyl residues were obtained from a preparation having 2, 7/10, 14 specificities. Just how the two cistronic gene products (LA and Four) are related is unknown. Presumably, two independent polypeptides are produced, which may then interact within the membrane's mosaic structure. Formation of a polycistronic messenger RNA and translocation of the gene products, in analogy with variable and constant regions of immunoglobulins, remain formal possibilities. Monospecific antiserums of greater affinity are needed as reagents to separate the specific antigens.

Transformed cells have tumor-specific antigens, yet tumors manage to evade an immune response, apparently by modulation, masking, or dilution of the cell surface antigen. R. Hyman (Salk Institute) described allelic forms of the normal thymus antigen theta in C3H and AKR strains of mice, use of cytotoxic antibody for immune selection of variant clones of lymphoid cell lines that have lost one or more detectable antigens, and cell fusion techniques to study regulation of antigen expression in hybrid cells. The relations among tumor-specific, histocompatibil-

ity, and fetal antigens remain to be clarified immunologically, chemically, and genetically.

Finally, P. Bretscher (Salk Institute) presented a speculative model for the development of generalized autoimmunity, in which both B and T cells would be required for induction of antibody production by foreign antigen, but in which only B cells would be necessary for maintenance of tolerance (paralysis of self-antigen). Such a model will have to take into account extensive data from autoimmune-prone NZB mice and from human patients and families with autoimmune disorders.

During the past decade, the study of immunogenetics has revealed several important biological phenomena. The synthesis of a single immunoglobulin polypeptide chain involves at least two genes, and an unknown mechanism generates extraordinary diversity in the variable region sequences of immunoglobulins. Mammalian histocompatibility antigens are extensively polymorphic, are coded by a genetically complex chromosomal region, and are linked to genes controlling immune responsiveness. An interacting system of two cell types is necessary to trigger antibody synthesis. The implications of these findings extend beyond the field of immunology to other genetic systems involved in differentiation.

GILBERT S. OMENN
Division of Medical Genetics, University of Washington, Seattle 98195
HUGH O. MCDEVITT
Division of Immunology, Stanford University, Stanford, California 94305

Forthcoming Events

October

1–4. National **Agricultural Chemical** Assoc., 39th annual, White Sulphur Springs, W.Va. (D. Hayley, NACA, Madison Bldg., 1155 15th St., NW, Washington, D.C. 20005)

1–5. Society of American **Foresters,** Hot Springs, Ark. (H. R. Glascock, Jr., SAF, 1010 16th St., NW, Washington, D.C. 20036)

1–14. International Assoc. of **Theoretical and Applied Limnology,** jubilee symp., Plon, West Germany. (W. Ohle, Max-Planck-Inst. für Limnologie, Postfach-165, 232 Plon)

2–3. **Air Pollution Medical Research** Conf., American Medical Assoc., Chicago, Ill. (F. W. Barton, Council on Environmental and Public Health, AMA, 535 N. Dearborn St., Chicago 60610)

2–4. **Distribution and Partition of Trace Elements and Origin of Volcanic Rocks,** intern. conf., sponsored by American Geophysical Union, Univ. of Rhode Island, Intern. Assoc. of Volcanology and Chemistry of the Earth's Interior, Newport, R.I. (American Geophysical Union, 1707 L St., NW, Washington, D.C. 20036)

2–4. **Soil Microcommunities,** 2nd conf., Syracuse, N.Y. (D. L. Dindal, Dept. of Forest Zoology, State Univ. College of Forestry, Syracuse 13210)

2–5. American **Vacuum** Soc., Chicago, Ill. (J. H. Singleton, Westinghouse Research Labs., Beulah Rd., Pittsburgh, Pa. 15235)

2–5. **Yeast Protoplasts,** 3rd intern. symp., sponsored by Spanish Biochemical Soc., Spanish Biological Soc., and Spanish Research Council, Salamanca. (Secretariat, Third Intern. Symp. on Yeast Protoplasts, Departamento de Microbiologia, Facultad de Ciencias, Universidad de Salamanca, Salamanca)

2–6. Modern Trends in **Activation Analysis,** 4th intern. conf., Sacly, France. (American Nuclear Soc., 244 E. Ogden Ave., Hinsdale. Ill. 60521)

2–6. **Environmental Health Aspects of Lead,** Commission of the European Communities and U.S. Environmental Protection Agency, Amsterdam, Netherlands. (Secretariat, Direction Protection Sanitaire, Commission des Communautés Européennes, 29, rue Aldringen, Luxembourg)

2–6. International Congr. on **Marine Corrosion and Fouling,** 3rd, Gaithersburg, Md. (H. C. Burnett, Room B264, Materials Bldg., Natl. Bureau of Standards, Washington, D.C. 20234)

2–6. **Remote Sensing of Environment,** 8th intern. symp., Ann Arbor, Mich. (Conference Dept., Extension Service, Univ. of Michigan, Ann Arbor 48104)

3–4. Symposium on **Aquatic Environment: Microbial Transformations and Water Quality Management Implications,** Office of Water Programs, U.S. Environmental Protection Agency, Washington, D.C. (L. J. Guarria or R. K. Ballentine, Fresh Water Pollution Control Section, Water Quality Protection Branch, Water Quality Non-Point Sources Control Div., OWP, EPA, Washington, D.C. 20460)

3–5. **Dietary Lipids and Postnatal Development,** intern. symp., Milan, Italy. (Miss H. J. Prain, Inst. of Pharmacology and Pharmacognosy, Univ. of Milan, Via A. Del Sarto, 21, 20129 Milan)

3–5. **Plastics, Electrical Properties and Applications,** Plastics Inst. of America, Rensselaer, N.Y. (R. K. MacCrone, Materials Div., School of Engineering, Rensselaer Polytechnic Inst., Troy, N.Y. 12181)

3–5. USA–Japan **Computer** Conf., American Federation of Informational Processing Socs. and Information Processing Soc. of Japan, Tokyo, Japan. (R. W. Rector, University Extension, Continuing Education in Engineering and Science, 6115 Mathematical Sciences Bldg., Univ. of California, Los Angeles 90024)

3–6. American **Roentgen Ray** Soc., Washington, D.C. (T. F. Leigh, Emory Univ. Clinic, Atlanta, Ga. 30322)

3–6. **Trends in Physics,** European Physical Soc., Wiesbaden, West Germany. (EPS, P.O. Box 39, CH-1213 Petit-Lancy 2, Switzerland)

3–9. Intern. Soc. of **Biometeorology,** 6th intern. congr., Stresa, Italy. (S. W.