ulus alone under such circumstances.

Levinson (*6*) has shown that this is also true for fusion when the modulation amplitudes of two sinusoidal components of a stimulus are both near threshold. He found that modulation amplitude of the combined stimulus had to be lower for fusion threshold than the modulation amplitude predicted on the basis of the individual components. The present analysis indicates that, for a given criterion of appearance, frequency must be higher than that predicted on the basis of individual components. Both of these differences—lower modulation amplitude and higher frequency—serve to reduce the appearance of flicker. It is evident that the appearance of flicker may be enhanced by the combination of sinusoidal components (*7*).

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Autoimmune Response in Rabbits Injected with Rat and Rabbit Liver Ribosomes

Abstract. Autoimmune hemolytic anemia and leukopenia, circulating autoantibodies for erythrocytes, leukocytes, and ribosomes; pathological changes in liver, spleen, heart, brain, and kidneys were produced in rabbits injected with rat or rabbit liver ribosomes. The hematologic and pathologic changes were reproduced by injection of anti-ribosomal serum into normal rabbits. The autoantibody specificity was related primarily to nucleotides and nucleosides.

Autoimmune human diseases (*1*) and experimental "autoallergic" diseases in animals indicate that autoimmunization occurs under certain conditions, although the nature and role of the autoantibodies have been questioned (*2*). An apparent contradiction exists in the facts concerning acquired specific immune tolerance (*3*) by which the body distinguishes "self" from foreign antigens, and that embryonic and adult animals can be made unresponsive to some foreign antigens (*4*). The dilemma can be resolved only by the production of autoimmune disease in experimental animals accompanied by circulating antibodies to tissue antigens of mesodermal origin and by reproduction of the pathology in other animals injected with serum from the actively autoimmunized animals.

Table 1. Hematology of a rabbit injected intravenously with serum from a ribosome immunized animal.

Days after injection	Hemoglobin (g)	Hematocrit (%)	Blood cells (thousands)		Reticulocytes (%)
			White	Red	
0	12.9	38	6.00	5730	0.5
1	12.0	36	7.10	5060	0.8
2*	14.7	43	9.00	5310	2.2
3	10.8	33	7.30	2710	3.0
4*	10.6	31	7.65	4180	6.7
5	8.2	27	5.20	3280	10.2
6*	<6.3	16	3.75	2280	7.8
7	9.3	30	5.40	3700	9.5
9	10.8	36	5.75	4290	9.0
12	12.0	41	6.20	4680	6.4
15	11.6	41	6.85	5240	3.3
19	11.1	39	5.05	5340	2.9
23	9.7	38	4.90	4130	2.2

* Free hemoglobin present.

Six rabbits were injected intramuscularly with rat liver ribosomes (*5*) in Freund's adjuvant. Dosage ranged from 83 to 140 mg of protein, representing approximately 50 percent of the material injected. Three animals survived 77 to 78 days. Between 70 and 77 days these animals had developed a marked hemolytic anemia and leukopenia. Data on one animal, representative of the group, showed a decrease in hemoglobin from 13.3 to less than 6.3 g; hematocrit index from 39 to 13 percent; red blood cell count from 5,500,000 to 2,430,000; and white blood cell count from 11,850 to 3,450. The anemia and leukopenia were verified further by differential blood smear examinations and evidence of red cell destruction in histologic sections of spleens. Autoantibody was indicated as early as 2 to 3 weeks after injection by agglutination of the red cells of the animals in antirabbit globulin chicken serum. Electrophoretic analysis of the serum showed an increase in the amount of gamma globulin and a decreased amount of alpha globulin and albumin. Blood cultures were consistently negative.

The animals were sacrificed and microscopic examination of the tissues showed marked loss of cytoplasm of liver cells and focal collections of plasma cells in the connective tissue septa of the liver. Spleens usually contained a perifollicular deposit identified histochemically as glycoprotein, which was not amyloid or hyaline. Focal myocarditis and various glomerulonephritic-like changes were observed. Some aspects of the pathology of the nervous system are compatible with changes observed in isoallergic encephalitis (*6*).

Table 1 shows representative findings in one of 12 rabbits injected intravenously with 1 to 5 ml of serum from donors injected with ribosomes. Hemolytic anemia, antiglobulin-positive reo cells, and hemoglobinemia were evident in 2 days. Anemia was maximal on the 6th day and evidence of it persisted for 23 days, at which time the animals were sacrificed. Leukopenia was moderate but definite by the 6th day. Occasionally, blood from these animals failed to clot after storage for 24 hours in the refrigerator. Histological changes practically identical to those described in donor animals, or in some cases more severe, were observed in recipients.

Autoantibodies were detected in the serum of rabbits injected with rat ribosomes as: (i) anti-rabbit ribosomes demonstrable as a hemagglutinin for human erythrocytes to which ribosomes were coupled with bis-diazotized benzidine (*7*); (ii) leukoagglutinins for rabbit leukocytes by the method of Wilson *et al.* (*8*); (iii) incomplete antibody for rabbit red cells by agglutination or normal erythrocytes previously sensitized by anti ribosomal serum, in antirabbit globulin chicken serum; and (iv) autoantiglobulins were detected in one animal as hemagglutinins to rabbit serum globulin fractions gamma, alpha IV, alpha IV-1, alpha IV-4, and beta (*9*). Autoantibodies were demonstrable in gamma globulin fractions separated by continuous flow electrophoresis. Intravenous injections of these fractions into rabbits produced the same hematological and histological changes as those obtained in the recipients of anti ribosome serum.

Rabbits injected with homologous rabbit ribosomes developed similar hematological, pathological, and serological changes after the 69th day. Rabbits given serum from these animals demonstrated the same phenomena as the recipients of anti-rat ribosome serum.

Tolerance should have been acquired by these animals to antigens of ribosomes, erythrocytes, leukocytes, and serum proteins. All of them are constantly present in large amounts and are available to immunologically competent cells and they can not therefore be classified as foreign antigens. These results therefore seem to warrant the claim of having achieved true autoimmunization. Reproduction of similar pathology in animals receiving serum or gamma globulin fractions containing autoantibodies provided evidence of a causal role for the circulating antibodies.

Antibodies for ribosomes, yeast, soluble RNA (*10*), and ribosomal protein (*11*) were demonstrable in anti ribosome serum and by skin tests. A relationship between antibodies for ribosomes, soluble RNA, and autoantibodies was shown by absorption. Inhibition tests indicated their specificity was for nucleotides, nucleosides, and bases, suggested that the mechanism of this autoimmunization involved these structures. Support for this theory was obtained from preliminary results with rabbits injected with soluble RNA in adjuvant, who developed practically all the aspects of animals immunized with ribosomes, while animals injected with ribosomal protein had few of the changes, and their sera reacted minimally with ribosomes. Rat liver nuclei stimulated production of antibodies to nuclei but no autoimmunization. Autoimmune human disease may possibly represent a response to nucleotides and nucleosides of viral or bacterial nucleic acids or to nucleic acids released from tissue under conditions, which perhaps like adjuvant, allow preservation of these configurations as antigens (*12*).

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Pigment Effector Cells in a Cnidarian

Abstract. Chromatophore complexes are described in the siphonophore *Nanomia cara*. The dispersion and concentration of pigment are related to variation in light intensity and do not appear to be endogenously influenced. The pigment, possibly an ommochrome, has an absorption maximum at 465 to 470 mμ.

Color change in animals is brought about by movement of pigment in specialized effector cells, the chromatophores. Five groups of animals, namely, echinoderms, annelids, mollusks, crustaceans, and vertebrates, are well known to possess this capacity (*1*); another case, generally overlooked, is that of certain Ctenophora (*2*). I am now able to report the occurrence of pigment effector cells in a member of the phylum Cnidaria, the siphonophore *Nanomia cara*.

Patches of pigment have often been described in physonectid siphonophores and in the case of *Nanomia* spp. the distribution of pigment is held to have taxonomic value (*3*). It has always been supposed that this pigment is immobile. Observations at the Friday Harbor Laboratories of the University of Washington in June 1961 showed, however, that the appearance of the patches changes in response to changes in light intensity (Fig. 1). During the day the pigment is dispersed and wide, often reticular, and patches of scarlet are visible to the naked eye; at night the pigment is concentrated into compact, plum-colored masses. A specimen with dispersed pigment, when placed in the dark, shows the fully concentrated condition within 45 minutes. Redispersion on exposure to subdued daylight takes place in about the same period. Strong light, such as the spot of a microscope lamp, brings about some degree of concentration. It is not known whether there is any form of endogenous control over the movement of pigment, but on various grounds this seems unlikely. Chromatophores kept in dim light, showing the partially dispersed condition, were exposed for 30 minutes to epinephrine (1 part in 10^5) and acetylcholine (1 part in 2×10^4), but no tendency to dispersion or concentration was detected in either case.

The patches vary in size. The small patches covering the male gonophores are probably single chromatophores. Larger patches such as those on either side of the velum in the nectophores are multicellular or syncytial complexes ("chromatosomes," *4*) representing up to 20 or 30 cells. The cells occupy an intraepithelial position within the ectoderm. Study of living material and of FWA-fixed ester-wax sections cut at 5 μ and stained with iron haematoxylin, reveals no cell membranes separating nuclei in the complex, but proof of syncytial organization will have to await studies with the electron microscope.

In color, the pigment resembles some carotenes and carotenoproteins but it

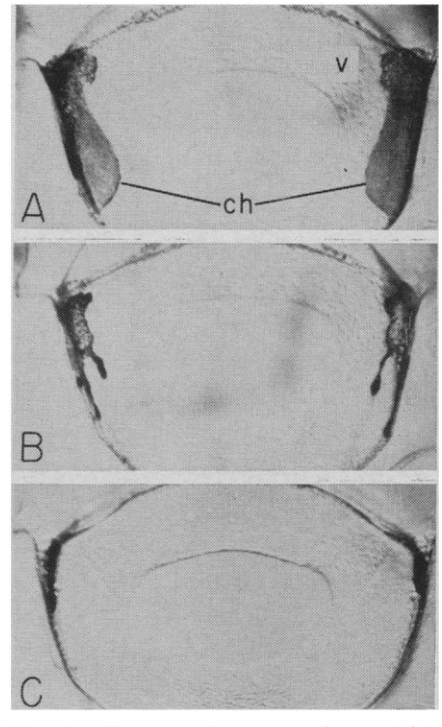

Fig. 1. Chromatophore complexes (*ch*) on either side of velum (*v*). *A*, pigment dispersed. *B*, same specimen, after 25 minutes in dark. *C*, another specimen, pigment fully concentrated.