In summary, it is possible to model with quantitative accuracy at least some postsynaptic responses using only the times of firing of presynaptic cells and a few straightforward assumptions about their effects. It remains to go from this point to a prediction of the resulting output impulse pattern of the postsynaptic cell.

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5. Delays and synaptic efficacies were measured in records from each penetration. Efficacies were obtained by measuring the amplitude of a synaptic potential from each driver cell and compensating each for its estimated antifacilitation. Time courses of synaptic potentials were measured for several ganglia and one with an appropriate shape was selected for a particular computer run. Calculated exponential tails were fitted to the synaptic potential since, in this region, errors introduced in measurement and by noise can add up significantly when many synaptic potentials are summed. Antifacilitation factors were assumed to be the same for all ganglia, since changes in them made little difference in the simulation. They were estimated from experiments where one or more driver cells were stimulated electrically by two pulses separated by a variable interval, from which synaptic potential amplitude was plotted against interval.
6. More mathematically, the theoretical synaptic potential amplitude for a given impulse was generated by multiplying a synaptic efficacy factor A_0, characteristic of each driver cell, by an antifacilitation factor $D = [r + 1 - \exp(-\Delta t/\tau)]$ where Δt is the time since the previous impulse in the same presynaptic unit, τ a time constant (a value of 100 msec was ordinarily used), and r a constant residual (usually set arbitrarily $= 0.1$). The theoretical membrane potential, $V(t)$, may then be described by:

$$V(t) = \sum_{i=1}^{4} \sum_{j=1}^{n_i} A^i{}_0 D^i{}_j \, f(t - [t^i{}_j + d^i]) \qquad (1)$$

where the jth impulse of the ith presynaptic cell occurs at time $t^i{}_j$ and is followed after a delay d^i by a synaptic potential whose waveform as a function of time θ from its beginning is given by $f(\theta)$. The function $V(t)$ was programmed on a PDP-8 computer made available by Dr. W. Simon of the Harvard Medical School under NIH grant 5-P07-FR00246-03.
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13 February 1969

Antiserum to Lymphocytes and Procarbazine Compared as Immunosuppressants in Mice

Abstract. *As an immunosuppressant procarbazine was as potent as an antiserum to lymphocytes in mice. Both agents significantly prolonged survivals of skin allografts by 4 to 6 weeks. At the maximum tolerated dosage, procarbazine suppressed both circulating hemagglutinins to sheep erythrocytes and plaque-forming cells in the spleen. The antiserum to lymphocytes reduced the numbers of circulating hemagglutinins and plaque-forming cells by 94 percent. Procarbazine was administered to mice for 3 weeks before their exposure to antigen. Exposure for only 9 days, commencing 48 hours before injection of sheep erythrocytes, was less effective in suppressing the titers of hemagglutinins.*

Antiserum to lymphocytes (ALS) is a potent immunosuppressant agent (*1*). Chemical immunosuppressants do not approach the effectiveness of ALS and are more toxic. However, Floersheim (*2*) reported that procarbazine a methylhydrazine derivative, can prolong the survival of skin allografts across strong histocompatibility barriers and even induce tolerance in adult mice if allogeneic lymphoid cells were injected as well. The advantages of a "chemical" ALS are obvious, and we now report results of a comparative study in which procarbazine compared favorably with ALS as an immunosuppressant.

The procarbazine [*N*-isopropyl-α-(2-methylhydrazino)-*p*-toluamide] was synthesized as the hydrobromide. It was dissolved in apyrogenic sterile water and administered within an hour by intraperitoneal injection. The concentration was adjusted so that the daily dose could be given in a volume between 0.2 and 0.3 ml, depending on the weight of the mouse. It was given in maximally tolerated doses, usually beginning 21 days before immunization or grafting. The reason for this long treatment is not known (*2*). The antiserum to lymphocytes against mice was produced in white New Zealand rabbits as described (*3*). Both the ALS and the normal rabbit serum (NRS), also obtained from white New Zealand rabbits, were sterilized by filtration under positive pressure through a series of Millipore filters. Two inbred strains of mice (Jackson Laboratories, Bar Harbor, Maine) were used for the skin-grafting experiments. The recipients were mature AKR/J male mice; the donors were C3H/HeJ male mice. The method of skin grafting was that described by Bliss (*4*).

All untreated grafted control mice rejected their allografts with a mean survival time of 12.5 days. Survival of grafts in a group treated with ALS (Table 1) was prolonged to 44.7 days. The group given maximum tolerated doses of procarbazine beginning on day −21 before grafting and continued to day 7 after grafting (the average total dose was 74 mg per mouse) had a mean survival time of the skin allo-

Table 1. Effect of ALS and procarbazine on skin-graft survival. The donors were C3H/HeJ males; the recipients were AKR/J males. The ALS (10 ml/kg, intraperitoneally) was given on days −2, −1, days 0, 3, 6, 9, and 12. The procarbazine was administered intraperitoneally as follows: 300 mg/kg from day −21 to day −19; 150 mg/kg from day −17 to day −12; 100 mg/kg from day −11 to day 0; and 50 mg/kg from days 1 to 7.

Treatment	Number	Mean graft survival (days)	$P = .05$ (days)
None	32	12.5	12.1 – 12.9
ALS	18	44.7	40.6 – 48.8
Procarbazine	10	56.6	51.5 – 61.7

Table 2. Effect of ALS and procarbazine of the primary hemagglutinin (on day 13) response of mice immunized with 0.1 ml of a 30 percent suspension of sheep red blood cells (SRBC). The NRS (10 ml/kg) was administered intraperitoneally on days −2, −1, and on days 0, 3, 6, 9, and 12. The ALS (10 ml/kg) was given intraperitoneally on days −2, −1, 0, 3, 6, 9, and 12. The procarbazine (150 mg/kg) was given intraperitoneally from day −21 to day −2; reduced dosage (50 mg/kg) was given from day −1 to day +7 (five of the eight had to cease treatment on day +1).

Immunization (day 0)	Treatment	Number of mice with reciprocal hemagglutination titer:									
		0	2	4	16	32	64	128	256	512	2048
SRBC	NRS	1		1	1		1	1		2	1
SRBC	ALS	4	1	2	1	1		1			
None	None	2									
SRBC	None				1	3	2	1	1		
SRBC	Procarbazine	8									
None	None	2									

grafts of 56.6 days. The treatment with procarbazine caused a weight loss averaging 11.8 percent of the starting weight, although no mice died. The animals recovered their weights rather quickly.

The effect of both agents on the primary hemagglutinin response to sheep erythrocytes was also striking in tests made with small numbers of AKR mice, but procarbazine was somewhat superior to ALS in its immunosuppressant effect. Eight mice that received the long treatment with procarbazine had no circulating hemagglutinins when tested at day 13 (Table 2). Four of ten mice treated with ALS had no circulating hemagglutinins although the others produced appreciable, but reduced, amounts of antibody.

In the plaque-forming cell test (*5*), treatment with ALS (10 ml/kg intraperitoneally from day −2 to day 3) suppressed the plaque-forming cells to sheep erythrocytes by 94.4 percent, when compared to controls treated only with the normal rabbit serum, the test being done on day 4. In a dosage of 150 mg/kg from day −21 to day −17, 100 mg/kg from day −15 to day −4, and 50 mg/kg until day +3 (all doses being given intraperitoneally and totaling approximately 60 mg per mouse), procarbazine suppressed all (100 percent) the plaque-forming cells in the spleen at day 4.

Procarbazine is an active agent which suppresses both cell-mediated immunity, as judged by prolongation of skin-graft survivals, and humoral antibody. It appears to completely suppress circulating antibodies to sheep erythrocytes in mice. It is difficult to claim that procarbazine is better than ALS as an immunosuppressant, as the potency and effect of ALS varies from batch to batch. It is theoretically possible to produce an even more potent ALS than was used in this study. The advantages of a chemical ALS over a heterologous serum are self-evident. We did not attempt to determine the minimum effective dose of procarbazine; in fact, the dosage was the maximum tolerated.

There is no immediate explanation for the need for a long period of treatment. In an experiment in which 150 mg of procarbazine per kilogram of body weight was given from day −2 to day 6, all the mice had circulating hemagglutinins to sheep erythrocytes at day 7, although the titers were lower than the controls.

The mode of action of procarbazine, like that of ALS, is unknown. Weitzel *et al.* (*6*) reported that it inhibited the transport mechanism of nucleosides into lymphocytes. Floersheim (*2*) also found procarbazine specific for lymphocytes, in that the total number in the circulation was reduced approximately 70 percent after 4 weeks of treatment. Thus procarbazine apparently specifically depresses lymphoid tissue in the mouse.

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1 November 1968; revised 11 March 1969

Photochemical Decomposition of DDT by a Free-Radical Mechanism

Abstract. *Both as a pure solid and in hexane solution, DDT readily decomposed when irradiated with ultraviolet light (2537 angstroms). Principal products identified by gas-liquid and thin-layer chromatography from irradiations of the solid phase were 1,1-dichloro-2,2-bis* (p-*chlorophenyl*) *ethane, 1,1-dichloro-2,2-bis*(p-*chlorophenyl*) *ethylene, and 4,4'-dichlorobenzophenone. 1,1-Dichloro-2,2-bis*(p-*chlorophenyl*) *ethane and hydrochloric acid were identified from irradiated solutions of DDT in hexane. On the basis of products obtained, quantum yields, scavenger experiments, and other chemical tests, a nonchain, free-radical mode of degradation is proposed.*

The resistance of DDT to degradation, as well as its effectiveness as an insecticide, is well known. The problem of DDT persistence in food products, soils, lakes, and the atmosphere is the result of the physical and chemical properties of the compound. We report here (i) the rate of ultraviolet degradation; (ii) the identification of the degradation products; and (iii) a proposed gross reaction mechanism of the photolysis.

Deposited as thin layers on the inside walls of quartz tubing, DDT was decomposed by ultraviolet light (2537 Å). After 48 hours of irradiation, 80 percent of the DDT was converted to a number of products including DDD, DDE, and DDC=O (*1*). To determine the mode of DDT decomposition, photochemical reactions were carried out in a quartz cell with DDT dissolved in *n*-hexane. Results from product identification, quantum yields, and radical-capturing compounds suggest that the photochemical degradation of DDT proceeded by a nonchain, free-radical mechanism.

Earlier work suggested that DDT could be decomposed by light. Lindquist *et al.* (*2*) reported that the insecticidal activity of DDT was reduced after a DDT solution was sprayed on surfaces exposed to sunlight. Wichmann *et al.* (*3*) found no effect of ultraviolet light on pure DDT, DDE, and DDC=O in the crystalline state. However, in benzene solution DDT decomposed and a yellow amorphic film was deposited after the solvent evaporated. Under the same conditions, DDE degraded more rapidly than DDT, but DDC=O was unaffected. Fleck (*4*) irradiated DDT in ethanol solutions and found that it decomposed to DDC=O in the presence of air. When the air was displaced from the cell with solution, a tetrakis (*1*) material was isolated.

To determine the extent of decomposition by ultraviolet light, uniformly ring-labeled ^{14}C and unlabeled carrier DDT were used. A standard solution of DDT (0.1 mg with a ^{14}C activity of 1.1 μc in glass-distilled benzene) was coated onto the inside surface of a quartz tube (2 by 35 cm). The solvent was removed by evaporation in a stream of dry air. The tube was sealed with serum caps, and flushed continuously with helium for 8 to 10 hours. The sample was then irradiated by four 15-watt germicidal, low-pressure, ultraviolet lamps (2537 Å). A yellow polymeric material which rapidly formed on the surface of the DDT (a phenomenon commonly occurring in photochemical reactions) eventually stopped further decomposition. In order to continue the reaction, the reaction mixture was dissolved with a small amount of diethyl ether. To evenly distribute the mixture over the