Direct interaction of the muramyl dipeptides with trehalose dimycolate in the therapeutic emulsions was essential for tumor regression. Two emulsions that were prepared separately, one containing trehalose dimycolate and one containing *N*-acetyldesmethylmuramyl-L-α-aminobutyryl-D-isoglutamine, and then mixed and injected into tumors did not produce significant tumor regression compared to controls (*19*). Only when the trehalose dimycolate and muramyl dipeptides were physically admixed with each other and with the oil, before addition of the aqueous solution of the emulsions (as for the experiments in Table 1), were the test materials active. This finding is similar to the results of a study of the physical interaction of trehalose dimycolate and endotoxic glycolipids (*20*). In that case it was proposed that water-soluble substances (such as the muramyl dipeptides in this study) complexed with the trehalose dimycolate through the trehalose portion of the molecule; the hydrophobic mycolic acid residues were envisioned buried in the oil droplets of the emulsions (*20*). These results indicate that a tertiary complex of muramyl dipeptide, trehalose dimycolate, and oil droplets is required for therapeutic effectiveness in the present system.

The synergistic antitumor effect of certain muramyl dipeptides and trehalose dimycolate described here may be useful for treating cancer in humans and animals. It must first be shown that these immunopotentiating agents can be used safely in humans and animals suffering from the stresses of cancer and its associated disease conditions.

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22. We are indebted to E. Ribi for his support and encouragement and to W. Bickel, R. List, and J. Kyle for superb technical assistance. This is Contribution 550 from the Institute of Organic Chemistry, Syntex Research.

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Visual Aftereffects Derived from Inspection of Orthogonally Moving Patterns

Abstract. *Alternate inspection of patterns moving in orthogonal directions induces an aftereffect in which a stationary test pattern seems to move in a new direction. This direction is the resultant of the two directions of aftereffect that would have arisen from separately inspecting each of the moving patterns. The direction in which objects appear to move, like their color and depth, can thus depend on a synthesis of unperceived components.*

When a pattern observed for a minute or so while moving is stopped, it appears to move for some time in the opposite direction (*1, 2*). This visual movement aftereffect (MAE) may be induced by linear, rotational, or radial (expanding-contracting) movement. It varies in strength as a function of numerous stimulus variables, including the direction of inducing movement and the luminance and contrast relationships of the moving and stationary patterns (*3*). The MAE has been interpreted in terms of an imbalance in the activity of neural units responsive to opposite directions of movement; units tuned to one direction are claimed to adapt negatively during prolonged observation, so when movement ceases, those tuned to the opposite direction are briefly more active (*4*).

In an experiment originally designed to test the hypothesis that the direction of the MAE is contingent on the orientation of bars in a moving grating, we followed the general procedure first described by McCollough (*5*) for generating a contingent aftereffect. Subjects inspected 45° bars moving continuously toward 135° [within a ring of anchoring dots (*6*)] in alternation with 135° bars moving toward 225° (Fig. 1A). The duration of each phase was 10 seconds. After 10 to 30 minutes of these alternating inspections, we replaced the moving grating with a stationary test pattern consisting half of 45° and half of 135° bars (Fig. 1A). We expected that, if the direction of the MAE were contingent on line orientation, the two sets of bars would appear to move orthogonally to one another, each in a direction opposite to that of the corresponding bars during inspection. None of the bars did so. Instead, all bars appeared to move together

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Table 1. Conditions, procedures, and results for seven series of observations.

Series	N	Moving pattern inspected to induce MAE (0° refers to movement horizontally to the right)			Stationary pattern to test MAE	Direction of resulting MAE
		Procedure	Pattern	Direction		
			Single direction			
1	20	2 minutes	45° bars or 135° bars	135° or 225°	45° bars or 135° bars	315° or 45°
			Alternation			
2	2	10 seconds each for 10 minutes	45° bars and 135° bars	135°, 225°	45° bars and 135° bars	0°
3	4	10 seconds each for 10 minutes	45° bars and 135° bars	135°, 225°	Dot pattern	0°
4	6	10 seconds each for 10 minutes	90° bars and 180° bars	180°, 270°	Dot pattern	45°
5	10	10 seconds each for 10 minutes	Dot pattern	135°, 225°	Dot pattern	0°
6	9	10 seconds each for 10 minutes	Magenta dots, green dots	135°, 225°	Magenta dots or green dots	330° to 345° 15° to 30°
7	8	5 seconds A, 15 seconds B	Dot pattern	A: 135°; B: 225°	Dot pattern	0° to 30°

in an entirely new direction—horizontally toward 0°. Thus, the direction of the MAE was not contingent on the orientation of the grating, but was unexpectedly opposite the resultant direction of the two alternating inducing directions of motion. Since this new effect has implications for an understanding of the mechanisms for motion perception and for synthesis of sensory information (*7*), we have made further observations to verify it and establish its generality.

The stimulus arrangement consisted of a circular aperture 4 deg (*8*) in diameter, in which the moving (inducing) and stationary (test) patterns were presented, and a concentric, stationary surround having an outer diameter of 7.2 deg. The inducing pattern moved alternately upward to the left (135°) and downward to the left (225°) (Fig. 1) at a uniform speed of 1.79 deg/sec. Viewing was monocular, and changes in direction were controlled by rotating a Dove prism that was interposed between the patterns and the eye. The moving patterns were on a transilluminated cylinder. Their luminance was about 60 cd/m^2, and that of the front-illuminated stationary test pattern and stationary surround about 11 cd/m^2.

Table 1 summarizes the conditions used to build up and test the MAE together with the number of subjects participating. Series 1 was simply a control, verifying that our experimental conditions could be used to produce a vigorous MAE of the usual kind, in which the direction of the MAE is opposite to that of the patterns used to produce it.

All subsequent experiments made use of alternate inspections of patterns moving in orthogonal directions. Each series was designed to rule out possible artifacts. Series 2 was an attempt to get around the possible restriction that a single visual test object, such as the bipartite test field (Fig. 1A), cannot appear to move in two different directions at the same time. We therefore introduced a new test pattern in which there were two separate gratings of smaller size and lower contrast. Even so, each grating exhibited a 0° MAE regardless of its own orientation. To verify this independence of orientation, series 3 replaced the grating test patterns with circular dots. Again, however, all dots were seen to move in the same direction, toward 0°. Series 4 shifted orientation and direction in the inducing gratings by 45°. Again, the dots of the test pattern showed a single direction of MAE, but the aftereffect was now oblique, in accordance with the 45° rotation of the field. This result shows that the effect cannot be attributed to our use of oblique inducing patterns in the previous experiments. Series 5 made use of dot patterns throughout (Fig. 1B). Again the result was the same; alternating inspection of dot patterns moving linearly toward 135° and

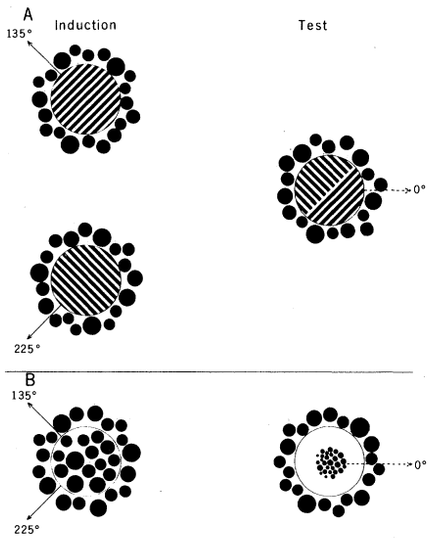

Fig. 1. The inducing and test patterns. The dots outside the circle are stationary at all times. They anchor and enhance the MAE (*6*). The solid arrows indicate alternating direction of inducing movement, and dashed arrows the direction of the motion aftereffect as seen inside the circle.

225° gave rise to an MAE in which the dots seemed to move in a direction opposite to the resultant of these two, namely toward 0°.

Carrying the resultant idea a bit further, we have shown that the perceived direction of the MAE can indeed be modified by altering the balance of the two components used to build it up. In series 6, we have taken advantage of the fact that a color-contingent effect influences the direction of the MAE (*9*). The 135° movement was viewed under magenta illumination (tungsten light through Kodak Wratten filter No. 32) in alternation with 225° movement under green (Wratten No. 57). After 10 minutes, the stationary dot test pattern was presented first in magenta and then in green illumination. All subjects reported a color-contingent difference in the direction of the MAE. Thus, the color-contingent effect was sufficient to cause a slight, but definite, deviation of the MAE from the resultant horizontal direction. In series 7, we returned to achromatic viewing conditions, but had our subjects spend three times as long inspecting dots moving in one direction (225°) as in the orthogonal direction (135°). The result was that, after 10 minutes of these alternate inspections, seven of the eight subjects reported a deviation of the MAE in the direction expected for the longer inspection (Table 1). (The remaining subject reported movement toward 0°.)

In a recent experiment, we induced an MAE through alternate inspection of 135° motion with the left eye alone and 225° motion with the right eye alone. The separate MAE's appeared to go as expected, toward 315° when the left eye was tested with a stationary pattern, and toward 45° when the right was tested. When tested binocularly, however, the MAE showed no trace of these separate effects; the test pattern appeared to move horizontally toward 0°. Thus, we conclude that neural substrates for three

different directions of MAE must have been established within the visual system. Only one direction was experienced at a time, as determined by the particular conditions of testing.

Taken together, our experiments show that the direction of the MAE can be synthesized from two or more components. This is a general finding independent of the specific patterns used to induce or to test the MAE. It is as if the motion-detecting cells of the brain pay no attention to the objects themselves, being concerned only with their direction of movement.

We cannot specify at this time the brain centers for the conscious and unconscious processing of motion information that our experiments have revealed. Present-day studies of single cortical cells have amply shown (*10*) that some of them are sharply tuned motion detectors. It remains, however, for electrophysiologists to identify cells or centers in which their signals are pooled to mediate new directions of motion.

On the psychophysical side, our findings are consistent with a recent report (*11*) that in the presence of a relatively strong MAE in one direction, a dot pattern of low contrast moving in another direction can seem to be deviated by as much as 10° in a direction toward that of the existing MAE.

Finally, the subjective effects that we observed are consistent with those reported in other perceptual domains. In normal color vision, for example, red and green lights can be combined to produce a yellow that appears as a new hue without any trace of its components (*12*). Similarly, a three-dimensional solid object can be made to appear in visual space by stereoscopic fusion of separately meaningless patterns presented to the left and right eyes (*13*). Our motion aftereffects may thus be added to a class of previously described instances in which the perception arises from a synthesis of unperceived components.

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An "Inhibitory" Influence on Brainstem Population Responses

Abstract. *Forward masking was used to obtain measurements of physiological masking and two-tone unmasking from short-latency evoked potentials and psychophysical responses in human subjects. The physiological results are in qualitative agreement with data on inhibitory phenomena in nonhuman auditory systems. The neural and behavioral data obtained thus far agree well.*

In vision, prominent edges often appear bordering regions of discontinuity in wavelength, intensity, texture, or other stimulus characteristics (*1*). Analogous "edge effects" occur in hearing at discontinuities (peaks or valleys) in the power spectra of sounds (*2*). These phenomena are apparently produced by a class of inhibitory mechanisms that effectively compare intensities in neigh-

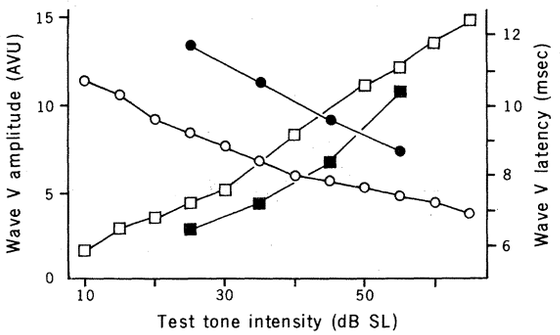

Fig. 1. Amplitudes (squares) and latencies (circles) of probe tone evoked wave V responses with and without masking. Filled symbols are for responses to masked tones. The amplitude measurements are in arbitrary voltage units; *SL*, sound level.

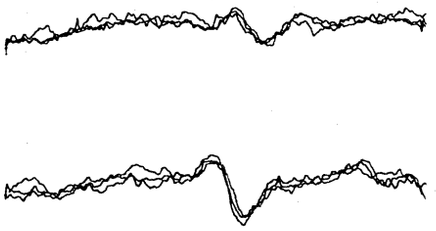

Fig. 2. Masked and unmasked probe evoked responses from one subject. Upper traces are responses to 25-dB probes in the presence of 50-dB maskers (re threshold in quiet). Lower traces show the effect of adding a 70-dB unmasker at 2.245 kHz. Positivity is upward; traces begin at probe tone onset and continue for 20 msec.

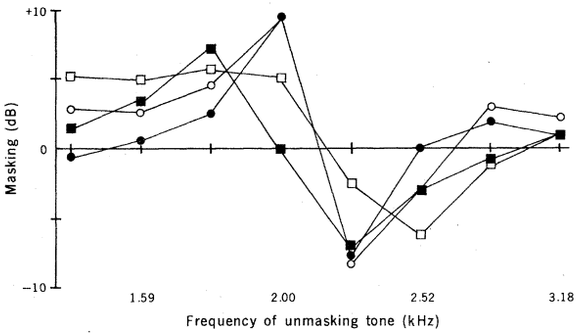

Fig. 3. Masking as a function of unmasker frequency. Open symbols are estimates based on wave V amplitudes (*13*). Filled symbols are psychophysical threshold shifts. Circles and squares denote two different subjects. Zero decibels refers to the masking produced by the masking tone alone. Unmasking is shown as negative masking.

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