

larger sample number must be used in the behaviors tests. Beside this, a second method to stress flies could be efficient to obtain a better result, too.

The results of the three pilots of this study showed that *D. melanogaster* is sensitive to alcohol and avoids this substance or dies when in concentrations higher than 5%. Besides this, when in starvation, flies of this species shows preference for substrates that contain palatable food, such as sugar. Results also indicate that *D. melanogaster* is sensitive to stressful situations, like related to immobilization and CO₂ anesthesia, and these situations could modify their behaviors to looking for food. This study shows a preliminary analysis of behavior of *D. melanogaster*. It is important to establishment of models for replacement of vertebrates in behavioral studies. However, to confirm the hypothesis it is necessary for a greater behavior analysis, with higher sample number.

Acknowledgments: We thank the technician Marcos Antonio Loureiro for the help in breeding the flies and for all the instructions.

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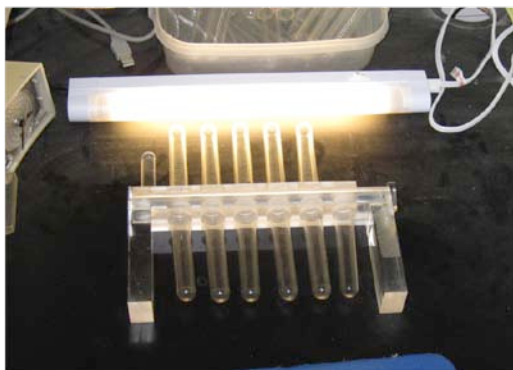
Mapping *Drosophila* phototaxis behavior mutants; Possibly extend method to genetic diseases in human families.

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Recombination based mapping traditionally measures distances between traits or markers by recombination fractions in order to map them. An alternative recombination based approach, based on localizing crossovers in intervals defined by markers having known locations, efficiently positions traits, including those previously difficult to map, to a chromosome section between such markers. This approach makes use of the fact that many gametes will carry a chromosome with either no crossover or only a single crossover. The class of non-crossover chromosomes can be used to map a trait to a specific chromosome (“not independent assortment” of the trait with reciprocal parental gametes). The class of gametes with a single crossover, identified by a change in phase at only a single interval between known markers, divides the chromosome into left and right portions; the sum of such divisions, over several progeny with single crossovers, can be used to localize the trait to a specific interval. For discrete dichotomous traits, such an approach is significant with relatively few progeny. For quantitative, or polychotomous, or weakly penetrant traits, the reciprocal single crossover-gametes for an interval can be typed for systematic differences in

phenotype, leading to left-right assignments of the locus relative to crossovers. Here I show *Drosophila* non-phototactic behavior mutants can be successfully mapped using this approach.

**Phototaxis counter current
apparatus, designed by Seymour
Benzer**



- Flies normally run towards light when agitated; flies that move to the top are shifted to the next tube, reach last tube on right after 5 moves to the light in 5 trials.

Figure 1.

y cv v f car parents

+ + + + +

(lower X chromosome has non-phototactic mutant)

- Sort progeny on counter-current apparatus for phototaxis behavior (progeny sort into tubes 0-5)
- Score numbers of each crossover type in each tube
- Graph results: compare phototaxis behaviors by their graph patterns. Map which interval changes pattern between black and white
- The non-crossover graphs show the different parental phototaxis behaviors
- The reciprocal single crossover progeny in each of the 4 intervals will show a parental behavior; the crossover in that interval will show the mutant to be either left or right of the crossover
- The results in all 4 intervals agree to the location of the mutant

Figure 2.

Males segregating the *norpA* mutation

00000 (white) and 11111 (black) are reciprocal non-crossover types (=y cv v f car and + + + + +, respectively)

01111 (white) and 10000 (black) are reciprocal single crossover types in the y-cv interval. Mutant maps there (crossover in interval can be to either side of mutant, therefore no difference in white and black graphs).

Crossovers in all 3 other intervals point to mutant at their left, confirming location.

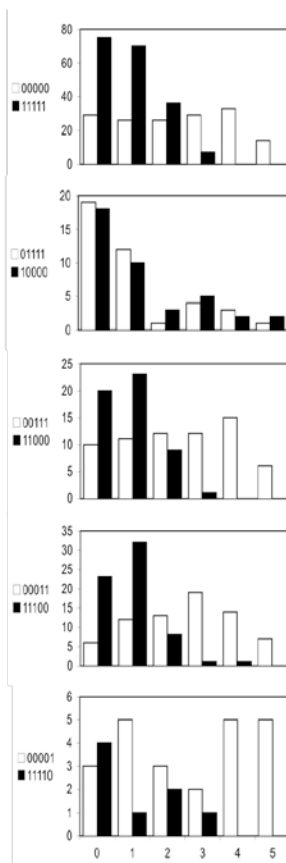


Figure 3.

Males segregating the *tan* mutation

00000 (white) and 11111 (black) are reciprocal non-crossover types (=y cv v f car and + + + + +, respectively)

01111 (white) and 10000 (black) are reciprocal single crossover types in the y-cv interval. Mutant maps to the right of that crossover location

00111 and 11000 are crossovers in the cv-v interval. Mutant maps there.

Crossovers in other 2 intervals point to mutant at their left, confirming location.

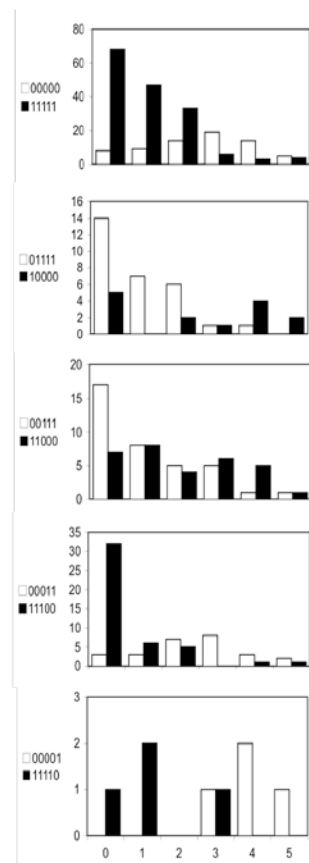


Figure 4.

The paper of Benzer (1967) is considered as the origin of neurogenetics. He identified four recessive X-linked mutants on the basis of abnormal phototactic behavior of failing to run towards light when agitated (Figures 1 to 4).. Two of these mutants, *tan* and *lozenge*, had additional phenotypic changes as well. In order to identify the genes involved and/or to confirm the importance of the *tan* and *lozenge* loci to phototaxis, the causative mutants were mapped using recombination with a well-marked X chromosome (*y cv v f car*) from a normal phototaxis background (Merriam and Benzer, 1969). Because the mapping data for the original four mutants are not available, the crosses were redone here for the *tan* and *norpA* mutants with stocks obtained from Bloomington. The *norpA* mutant was recovered in a follow up screen for non-phototaxis mutants using an apparatus shown below (Merriam unpublished, cited in Hotta and Benzer, 1970; and Benzer, 1973). The *norpA* gene is located at 1-7 between *y* and *cv*; the *tan* gene is located at 1-27 between *cv* and *v*. These two cases provide sufficient examples for the method of using recombination to identify the locations of risk alleles for behavioral, quantitative, or otherwise individually non-obvious phenotypes. Data are available on request.

Table 1. The predicted frequency of sperm carrying 0, 1, 2, 3, 4 or 5 crossovers per autosome, obtained from applying the calculations of Figure 3 to the observed exchange frequencies in Figure 2. The % do not always sum to 100 as explained in Figure 2. *means some possible but less than 1%.

Chromosome	% gametes with each number crossovers					
	0	1	2	3	4	5
1	7	26	35	22	6	*
2	10	32	36	18	4	*
3	12	35	36	15	2	
4	18	43	31	7	*	
5	16	41	33	8	*	
6	17	41	32	6	*	
7	17	41	32	6	*	
8	23	48	27	3		
9	20	44	30	6		
10	22	46	28	4		
11	22	47	28	4		
12	18	27	33	25		
13	26	49	24	1		
14	49	50	1			
15	25	48	23	1		
16	26	48	24	2	*	
17	25	48	25	2		
18	30	50	20	*		
19	25	50	25	*		
20	30	50	20	*		
21	50	50				
22	47	48	2			

How many crossovers are observed/expected in human chromosomes?

Because of the abundance of DNA markers every human family has the potential to be fully informative for every chromosome, *i.e.*, every chromosome can be well-marked for heterozygosity with sufficient intervals analyzed to recognize every crossover. To determine whether such an approach would be feasible for mapping human traits, I estimated the frequency of non-crossover, single crossover, and multiple crossover bearing gametes for human chromosomes from the literature on the observed distribution of chiasmata in sperm (Table 1).

Those recombination levels are in the range to make this a workable approach for human family studies with three generations or more. Their application to studies on common disorders may be helpful in finding high risk low frequency causative alleles or in assessing the relative importance of chromosome sites that are associated with risk alleles.

Literature cited: Benzer, S., 1967, Proc. Natl. Acad. Sci., USA 58: 1112; Benzer, S., 1973, Scientific American 229: 24; Hotta, Y., and S. Benzer 1970, Proc. Natl. Acad. Sci., USA 67: 1156; Merriam, J., and S. Benzer 1969, Genetics 61: s40.