when the cells actually attained their final positions.

This study establishes that neurons generated on a day early in development eventually occupy a relatively narrow zone of the mature cortex, while those generated on a later day are eventually distributed over a somewhat wider zone; also, neurons born 8 to 10 days apart overlap somewhat in position along the radial axis (Fig. 2). One reason for the wide distribution of cells generated simultaneously may be differences in rates of migration. Slower-moving neurons might reach the cortex when it had increased several hundred micrometers in thickness by the addition of neurons that were generated later but had migrated faster. Within a population of simultaneously labeled cells, the slower-moving neurons would presumably take more superficial positions than the faster-moving ones. Indeed, initial examination of monkey embryos killed at shorter intervals after injection of [^{3}H]dT suggests that some labeled neurons reach the outer border of the cortical plate in less than 3 days, whereas others labeled simultaneously take 7 or more days to reach a comparable destination (*10*). Variations in the length of the cell generation cycle also could influence eventual neuron position in the cortex, as might differences in the detailed aspects of cell interaction during migration (*11*).

Autoradiographic results in the brain of this primate corroborate in general the "inside-out" pattern of cell disposition described for rodents (*3*). Initial observations suggest that cells in other cortical areas in the monkey behave similarly, although on slightly different time schedules (*10*). Comparison of the data in Fig. 2 with studies in mice (*12*) shows that simultaneously generated neurons in the monkey eventually become confined to relatively narrow strata of the cortex; that is, the "inside-out" principle is more rigidly followed in the monkey. This may be the developmental basis for the sharper boundaries of cortical layers in the visual cortex of adult primates.

The monkey neocortex acquires its full complement of neurons at relatively early stages of gestation. The last cortical neurons are generated close to birth in mice and rats, and cortical genesis continues for a few days after birth in the hamster (*3*). In contrast, the last neurons destined for the primary visual cortex are generated around E100 in the monkey, that is, about 2 months before birth. It is probable that other primates, including man, also acquire a full complement of neocortical neurons well before birth.

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Deuterium Oxide Effect on Temperature-Dependent Survival in Populations of Drosophila melanogaster

Abstract. *A comparison of the mean life-spans for populations of* Drosophila melanogaster *at 10°, 20°, 25°, and 30°C maintained on media prepared with distilled water and with 50 percent deuterium oxide shows that deuteration decreases longevity at all four temperatures. The magnitude of the difference between the mean survival times of populations maintained on deuterated and nondeuterated media is inversely related to temperature between 10° and 30°C.*

We have compared the survival of *Drosophila melanogaster* (Oregon-R) males maintained at 10°, 20°, 25°, and 30°C on medium (Carolina Instant Medium, Carolina Biological Supply) prepared with 50 percent D_2O with those maintained on medium prepared with distilled H_2O. The mean life-span of these *Drosophila* populations at 20°C was reduced from 85 to 29 days on a diet prepared with 50 percent D_2O. Furthermore, we found that reducing the temperature to 10°C caused a decrease in mean survival time from 29 to 7 days for populations maintained on the D_2O medium, whereas survival time was increased from 89 to 112 days for populations supplied with distilled H_2O medium. Raising the temperature from 20° to 25°C for populations supplied with D_2O medium increased survival from 29 to 36 days. At 30°C mean survival time dropped

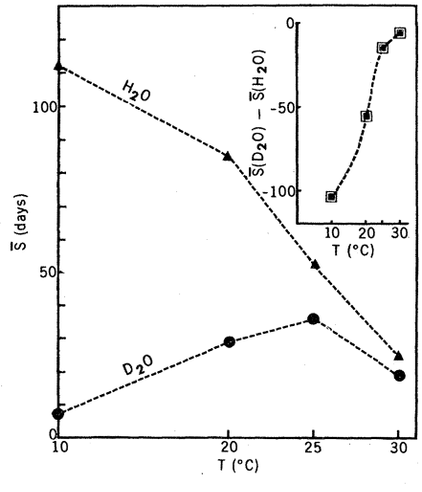

Fig. 1. Mean survival time ($\bar{S}$) in populations of *Drosophila melanogaster* (Oregon-R) males maintained from 1 day of age on Carolina Instant Medium prepared with distilled H_2O or with 50 percent D_2O at temperatures (T) of 10°, 20°, 25°, and 30°C. The light-dark cycle was 12 hours-12 hours. Flies were reared at 20°C on standard corn meal–molasses agar. Ten tubes of 20 flies each were used for each determination of $\bar{S}$. (Inset) Difference between mean survival times for populations on D_2O medium [$\bar{S}(D_2O)$] and H_2O medium [$\bar{S}(H_2O)$].

to 19 days. Survival time in populations maintained on the H_2O medium decreased with increasing temperature from 89 days at 20°C to 51 days at 25°C and 25 days at 30°C.

The differential effect of H_2O and D_2O on survival [mean survival time on D_2O medium minus mean survival time on H_2O medium (Fig. 1, inset)] decreased with increasing temperature, becoming very small (6 days) at 30°C.

Deuteration of biological systems has been shown to decrease the rates of essentially all biological processes for which its effect has been studied (*1*). The effect of deuterium has been compared to the effect of decreasing temperature on temperature-sensitive processes; this has been referred to as the "low temperature equivalence" hypothesis (*2*).

If, as has been postulated (*2*), deuteration of biological systems with D_2O decreases the "apparent biological temperature," this mimicry may be expected to extend to survival time in populations of poikilothermic organisms such as *Drosophila*.

It has been suggested that decreasing temperature increases survival time in populations of poikilothermic organisms either through a decrease in the rate of senescence [the "rate of living theory" (*3, 4*)] or through a temperature-dependent change in the "vitality threshold" (*5*). These ideas have received much attention since the early work of Loeb and Northrop (*6*) and Alpatov and Pearl (*4*). Maynard Smith (*5*) has taken exception to the idea that the temperature effect on survival in populations of poikilotherms is due to a decreased rate of senescence at lower temperatures. On the basis of the effect of temperature change during adult life in populations of *Drosophila subobscura*, he proposed that the rate of senescence is unaffected by temperature, but the "vitality threshold" is temperature-dependent.

Strehler (*7*) suggested that decreasing body temperature could result in a "considerable increase in longevity" in homeothermic organisms if a means could be found to compensate for any intolerable temperature-dependent decrease in the rates of physiological processes. Since lowering the body temperature of homeotherms by changing the environmental temperature is not feasible, the desired result may be achieved by chemical mimicry without resorting to manipulation of body temperature.

Our findings place in question the notion of deuterium mimicry of temperature effects on biological systems as well as the notion that temperature affects survival in populations of poikilotherms in a way analogous to its effect on chemical reactions.

The fact that the survival time of *Drosophila* maintained on D_2O decreases with decreasing temperature suggests that effects of deuteration on survival may be due to a binding phenomenon, decreasing the activity of hydrogen at sites of deuteration. Changes in the structure of water due to deuteration may decrease cellular, molecular, and ionic activities to a level which leads to an increase in the probability of death in the deuterated population.

It is possible that the decrement in survival time at any one temperature for flies supplied with medium prepared with 50 percent D_2O may be due to a toxic effect of D_2O at high concentrations which obscures the primary temperature mimicking effect. However, Pittendrigh *et al.* (*2*) demonstrated temperature mimicry of deuterium with 100 percent D_2O.

In our judgment, our findings demonstrate that temperature effects on survival in populations of *D. melanogaster* are not due simply to changes in the rates of temperature-sensitive biological processes of the classical sort, since the survival time of flies maintained on deuterated medium increases with increasing temperature.

Remaining open is the question of whether the deuterium effects observed by us as well as by others (*1, 2, 8*) result from modifications in the properties of the aqueous solvent or from increased deuteration of organic biomolecules.

The effects of deuterium on circadian oscillations (*2*) and the suggestion (*9*) that changes in the temporal organization of biological process may be a signal factor in senescent deterioration indicate to us that differential effects of deuterium on linked biological oscillations may be at the root of the seemingly paradoxical biological effects of deuterium.

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Reduction of Ferricytochrome c by Some Free Radical Agents

Abstract. *Fast pulse radiolysis and kinetic spectroscopy were used to rapidly generate a variety of free radicals in situ and study their reactions with ferricytochrome c in the time range 10^{-6} to 1 second. The radicals included* t-*butanol, which is inert to ferricytochrome c; malate, lactate, and ethanol, which react with it relatively slowly but are completely utilized in reducing it to ferrocytochrome c; and hydrated electrons and hydrogen atoms, which react with it very rapidly but yield ferrocytochrome c only in part, showing intramolecular consecutive reactions and further attack on the ferrocytochrome c protein. From a detailed comparison between malate and hydrogen atoms it is argued that malate reacts directly and selectively with a specific part of the ferricytochrome c surface while hydrogen atoms react with other parts of the protein too, yielding radicals which in part transfer intramolecularly to yield ferrocytochrome c.*

In the structure of ferricytochrome c (CIII) the protein wraps the ferri-heme (*1*) so that only one edge of the porphyrin is exposed, forming some 3 percent of the total surface area of the enzyme. Reduction of CIII to ferrocytochrome c (CII) might proceed by direct reaction of the reducing agent with this defined region or its immediate surroundings, or by reaction with a site or sites elsewhere on the protein followed by intramolecular electron equivalent transfer to the iron moiety (*2*).

The reduction of CIII to CII by