Further analysis of such variants should clarify the role of temporal genes (*10*) in determining developmental processes.

The sharing of a common developmental program by two apparently unlinked structural genes implies the existence of additional genetic factors determining the program itself. For this reason it will be of interest to identify mutations simultaneously affecting the development of these two enzymes.

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4. Electrophoretic studies were performed with samples of 105,000*g* supernatant fractions prepared from the tissue homogenates described in Fig. 1. Electrophoresis was carried out at *p*H 8.1 at 300 volts (1 ma per tube) for 60 minutes at 0°C. Gels containing 7.5 percent polyacrylamide were prepared according to the method of J. T. Clarke [*Ann. N.Y. Acad. Sci.* **121**, 428 (1964)], except that the gel buffer contained 29 g of glycine and 12 g of tris per liter. β-Galactosidase activity was visualized with the substrate 4-methylumbelliferyl-β-D-galactoside [L. Fluharty, E. L. Lassila, M. T. Porter, H. Kihara, *Biochem. Med.* **5**, 158 (1971)], and β-glucuronidase activity with the method of Hayashi [M. Hayashi, Y. Nakajima, W. H. Fishman, *J. Histochem. Cytochem.* **12**, 293 (1964)].
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11. The reproducibility of enzyme assays for individual animals was determined for animals 5 days of age and for adults. At both ages, the standard deviation of determinations of β-glucuronidase and β-galactosidase was 8 to 13 percent for liver and heart and 3 percent for brain. Since the variance was quite reproducible and agreed with variance determinations from other experiments, pooled samples were used for the remaining time points. The estimated standard errors of our measurements are ± 5 percent for liver and heart and ± 1.5 percent for brain.
12. Protein was determined by the biuret method [E. Layne, *Methods Enzymol.* **3**, 447 (1957)], with bovine serum albumin as standard.
13. We are indebted to the staff of the Jackson Laboratory for helping to gather and analyze the samples. This work was supported in part by research grants GM 18484 from National Institutes of Health and NP-29B from American Cancer Society.

30 May 1972

Mobility Gaps: A Mechanism for Band Gaps in Melanins

Abstract. *The semiconductor behavior of melanins is reviewed and compared with quantum mechanical models of conduction in amorphous solids. The available data are consistent with extensions of Mott's basic model for amorphous semiconductors, whereas they are inconsistent with crystalline semiconductor models. An investigation of the specific conduction mechanisms operative in melanins in terms of the amorphous model should reveal important aspects of the band structure.*

Melanins are good electron acceptors and have semiconductor properties (*1*), which appear to be important in the midbrain structures (*2*). In relation to these electronic properties, Cotzias *et al.* (*2*) noticed that both naturally occurring and drug-induced dyskinesia occur in species which possess visible melanin in the substantia nigra. Such data suggest that melanins have a more fundamental biological role than that of providing pigmentation or an ultraviolet sunscreen (*3*). For this reason a model of the electronic structure of melanins is of more than academic interest.

An analysis of data on melanins and melanin-containing systems suggests that the electronic properties of melanins can best be explained in terms of a band model for semiconduction in amorphous materials. The electronic properties of melanins have been of considerable experimental interest. Blois (*4*), in addition to measuring other solid-state properties, investigated the possibility that melanins are intrinsic semiconductors. Blois (*5*) has pointed out that inconsistencies exist between the data on pure melanins and interpretations based on crystalline models of semiconductor behavior. Interpretation has, therefore, been ambiguous, even for the most elementary system, purified melanin. A quantum mechanical calculation based on the monomer unit indole-5,6-quinone was presented by Pullman and Pullman (*1*) in an effort to calculate the band structure of melanins.

It is necessary to differentiate between the melanin macromolecule and more complex systems, such as melanin-containing organelles. However, in some systems of greater complexity the electronic properties of melanin may dominate the behavior of the system in a particular situation. Pant and Rosenberg (*6*) found that the photoconductivity through a Fe^{3+}-completed oxidized cholesterol bimolecular membrane reaches a peak as the electron donor concentration is increased, which indicates a band-filling mechanism. The interaction of certain electron-donating drugs, such as chlorpromazine, with melanin has been shown to follow a similar band-filling pattern (*7*). The discussion in this report is restricted to the macromolecular form of melanin unless otherwise noted.

The basis for most current research in the quantum mechanical description of amorphous materials was presented by Mott (*8*), in terms of the exact solution of the one-dimensional random square well model for the single-particle wave functions. Mott used perturbation theory to show that the one-dimensional results should extend to three dimensions.

The solution of the random square well model yields a set of energy levels similar to those of crystals, but with some interesting differences (*9*). For example, in amorphous materials there is an essentially Gaussian density of states (*8*, *10*). The states under the peak are extended, whereas the states under the tails are localized. An extended state is one in which the electron has "essentially" the same probability of being found anywhere in the crystal. Conversely, in a localized state the electron is essentially restricted to a local volume. The existence of tails of localized states is peculiar to the band model of amorphous materials; in crystals the band edges are more sharply defined (*8*). The mobility of electrons in localized states is less than that in extended states, since electrons in localized states must depend on tunneling or phonon-assisted hopping to change their states. Extensions of Mott's model have appeared in the last 2 years (*9*, *11*). The result for amorphous semiconductors is a model of conductivity based on mobility of electrons in localized states rather than on a gap in the density of states, which is characteristic of crystalline solids. The conductivity changes as the highest occupied level is moved through regions of extended and localized states by the action of doping.

Some of the inconsistencies between the melanin data and theories of conduction based on crystalline semiconductors are removed when the amorphous band model is used. The existence

of a mobility gap implies an activation energy without the electron spin resonance threshold at low temperatures (*11, 12*), in agreement with the fact that no threshold was found (*5*). This fact was considered paradoxical since sharp thresholds are observed in crystals (*5*). In melanins and in crystals conductivity increases with the absorption of light. This may occur by parallel mechanisms, increased mobility: in melanins by the promotion of electrons from localized states to extended states, and in crystals by the promotion of electrons across the gap in the density of states. The rise in conductivity when a voltage is applied, which was also considered anomalous (*4*), may be explained in terms of (i) an increase in the kinetic energy of the electrons with respect to the potentials within which they are trapped, leading to higher mobility and promotion to excited states (*8*), or (ii) field-assisted emission from acceptors, which produces exponential behavior in the current-voltage characteristics (*13*).

In addition to removing apparent inconsistencies, the amorphous band model may be instrumental in unraveling the band structure of melanins. In fact, the rise in conductivity with applied voltage may give information about the trap density distribution (*14*). Hill examined the conductivity of amorphous materials as a function of the temperature, applied field, and distribution of hopping sites, and concluded that the conductivity (σ) is related to the temperature in a linear manner if $\ln\sigma$ is plotted against $T^{-1/n}$, where the value of n depends on the specific form of the electron-phonon interaction and the distribution of hopping sites. It is perhaps helpful to point out that a detailed analysis of the conductivity of melanins allows us to make statements about their band structure; that is, there is an intrinsic relationship between conductivity and band structure. If the band structure is known, it is possible to deduce the changes in conductivity with doping. These predictions can then be compared with the experimental data in a quantitative way. By comparing the conductivity of melanins as a function of temperature and applied field with the predictions of Hill's theory, we should obtain a greater insight into the band structure of melanins.

The biological applications of the theory of amorphous semiconductors begin with the agreement between theory and experiment. Cope (*15*) pointed out that inconsistencies also exist between the behavior of proteins and other biological macromolecules and predictions based on the crystalline model. Perhaps the amorphous theory is applicable here also. The role of electron-phonon interactions is fundamental in the present theory of amorphous semiconductors. McGinness and Proctor (*16*) propose that melanins may de-excite certain biological molecules by converting electronic energy to heat.

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Human Lactational and Ovarian Response to Endogenous Prolactin Release

Abstract. *Radioimmunoassayable prolactin rises in postpartum women during nursing and after intravenous thyrotropin-releasing hormone (TRH). Prolactin release induced by TRH can be dissociated from the postsuckling response. In addition to this, increases in endogenous prolactin secretion are followed by marked breast engorgement and milk letdown, especially after intravenous TRH. In this group of breast-feeding women, vaginal smears remained atrophic even up to 410 postpartum days. Prolactin appears to influence the production of breast milk, and the maintenance of a regular nursing pattern seems to promote the maintenance of ovarian unresponsiveness to circulating gonadotropins.*

The identification and isolation of human prolactin has led to studies of its secretory pattern under various physiological circumstances, by using a specific radioimmunoassay (*1*). Little is known, however, of the site and the mode of action of this human pituitary hormone. Increased concentrations of prolactin have been found in the peripheral plasma and amniotic fluid of pregnant women (*2*). Postpartum, increased prolactin concentrations are found in lactating women on each occasion within 30 minutes of the onset of nursing. This response is variable and in most instances absent after the 60th postpartum day, despite the presence of continued milk production and letdown (*2*).

The intravenous injection of the synthetic tripeptide pyroglutamyl-histidyl-prolinamide or thyrotropin-releasing hormone (TRH) is followed by significant increases in plasma prolactin concentrations (*3*). Prolactin release under these circumstances occurs as a direct effect of TRH on the anterior pituitary (*4*). The present studies were performed to determine the responsiveness of the

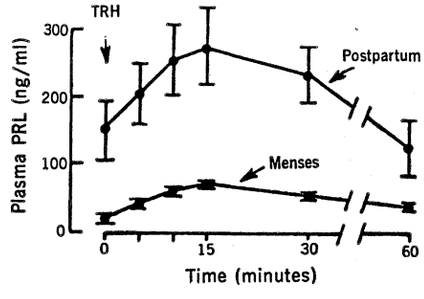

Fig. 1. Plasma prolactin (*PRL*) concentrations after intravenous TRH in five menstruating women and eight lactating women 3 days postpartum. All values are expressed as mean ± the standard error.