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

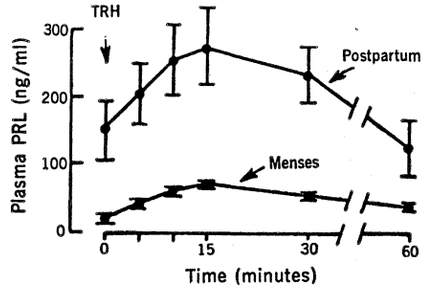

Fig. 1. Plasma prolactin (*PRL*) concentrations after intravenous TRH in five menstruating women and eight lactating women 3 days postpartum. All values are expressed as mean ± the standard error.

Table 1. Mean plasma prolactin levels, in nanograms per milliliter, before and 30 minutes after nursing. Values are means ± standard errors. N.S., not significant.

Phase	Interval	Before nursing	After nursing	No. of studies	*P*
I	Days 0–7	138.4 ± 14.2	198.9 ± 17.6	10	< .02
II	Days 8–60	30.9 ± 7.5	160.5 ± 46.0	12	< .01
III	After day 60	25.7 ± 7.0	60.4 ± 18.9	20	N.S.

postpartum pituitary of lactating women to the intravenous administration of TRH in an attempt to determine the relationship between postpartum prolactin release and mammary function.

Synthetic TRH (lot No. 844-8906, Abbott Laboratories) was administered intravenously to healthy, nonobese, parturient, lactating women between the 3rd and the 410th postpartum days. A group of healthy, nonobese female volunteers between 19 and 21 years of age served as controls. Between 100 and 500 μg of TRH dissolved in 10 ml of physiologic saline was administered as a single intravenous bolus over 30 seconds through an indwelling catheter in an antecubital vein. The TRH dose was calculated at 5 μg per kilogram of body weight for controls and 10 μg per kilogram of body weight for parturient women. We have shown that a maximal prolactin response can be expected from as little as 25 μg of TRH in only 40 percent of cases; therefore, the above dosages were chosen to assure us of a maximal prolactin response in each study.

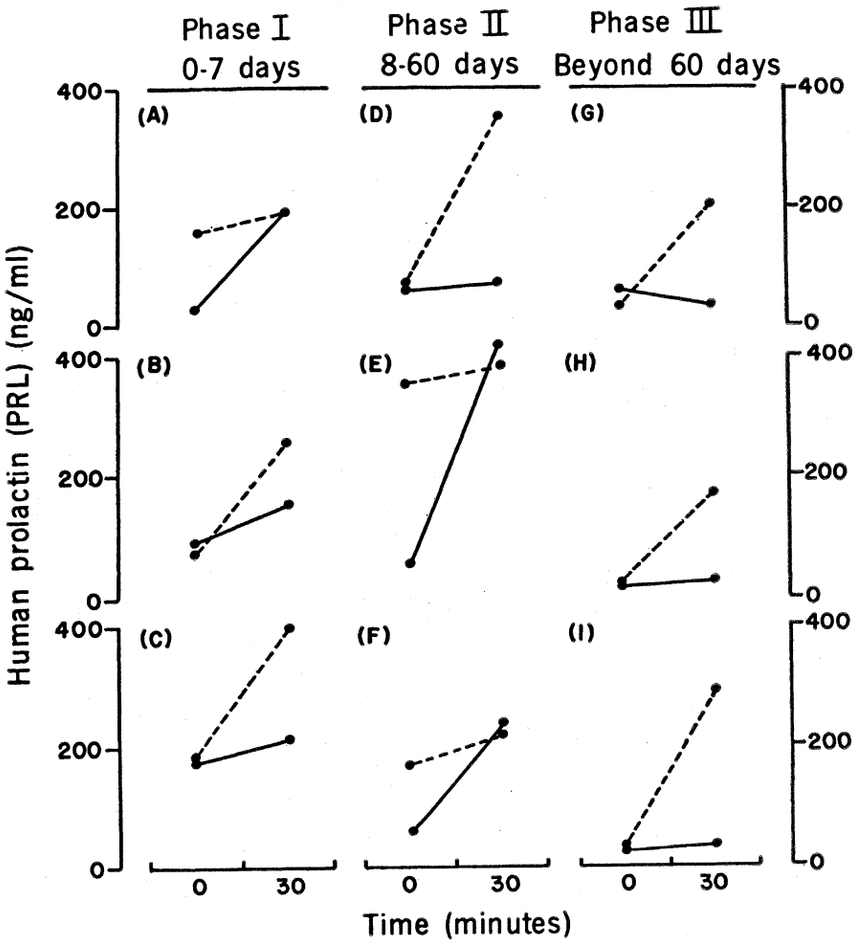

Fig. 2. Plasma prolactin concentrations in eight lactating women at three specific postpartum intervals. Prolactin was measured before and up to 30 minutes after nursing began (solid lines) and after intravenous pyroglutamyl-histidyl-prolinamide (dashed lines). The exact postpartum study times were as follows: (A) 4 days; (B) 6 days; (C) 3 days; (D) 56 days; (E) 21 days; (F) 42 days; (G) 70 days; (H) 84 days; (I) 410 days. (E) and (F) are the same woman. All patients received 200 μg of TRH except for patient (I), who received 500 μg of TRH.

In the women with regular menstrual cycles, blood was drawn in cold heparinized tubes before and again at 5, 10, 15, 30, and 60 minutes after the injection of TRH. In lactating women, blood was drawn immediately before and 30 minutes after nursing began. The TRH was injected as soon as possible after the 30-minute postnursing sample. Human prolactin was measured by a modified double antibody radioimmunoassay (*2*) with a sensitivity of 1.5 ng/ml. [^{125}I]Prolactin was prepared by the method of Hunter and Greenwood (*5*). There was no cross-reactivity in this assay with thyrotropin, growth hormone, or human placental lactogen. Nausea, vomiting, and urinary urgency have been reported following intravenous TRH. None of these side effects was observed in our study patients.

Intravenous TRH in five menstruating women provoked a maximal rise in prolactin (40.7 ng/ml) 15 minutes after injection as shown in Fig. 1. When repeated at midcycle (9 to 13 days) intravenous TRH produced a similar rise in prolactin. In each case, prolactin returned to pretest concentrations by 60 minutes. Signs or symptoms of breast changes were not observed after TRH-induced prolactin release.

Prolactin gradually rises throughout pregnancy, and after delivery the basal prolactin gradually falls toward prepregnant concentrations by 7 days (*2*). Nursing during this time produces significant elevations in prolactin. This response to nursing can be divided into three distinct phases depending upon the length of time postpartum, as shown in Table 1.

Phase I is characterized by a high basal prolactin followed by a small but consistent rise 30 minutes after nursing. In phase II, basal prolactin is still somewhat elevated (mean, 39 ng/ml) compared to the normal female controls (0 to 28 ng/ml), but the prolactin increment in response to suckling can be as much as 50 times the basal concentration (*2*). Phase III is defined as that period beyond the 60th postpartum day when the prolactin levels increase inconsistently after nursing.

Intravenous TRH in seven lactating women in postpartum phase I produced a marked increment in prolactin concentration. The postpartum prolactin increment following TRH was similar to that observed in menstruating women (Fig. 1), but the absolute increment was significantly greater than during menses.

It was possible to dissociate the TRH-induced prolactin response from the prolactin response to suckling. This is shown in eight lactating women between the 3rd and 410th postpartum days (Fig. 2). The TRH was injected between 5 and 15 minutes after the completion of a 30-minute nursing period, depending on the time needed to return the infant to the nursery. In phase I, nursing resulted in a significant rise in prolactin with a second rise after the injection of TRH. In patient A, however, the post-TRH rise was small owing to the very high basal level of prolactin remaining after nursing. The prolactin response to suckling in phase II decreased between 21 days (Fig. 2E) and 56 days (Fig. 2D); the TRH-induced rise persisted. Only small prolactin responses to suckling were observed beyond 60 days postpartum, yet TRH continued to stimulate considerable prolactin release.

Each volunteer was breast-feeding her child on a 4-hour schedule. Prior to testing with TRH, breast engorgement between feedings had never been a cause for complaint. Breast engorgement with bilateral milk letdown was observed in each woman approximately 2.5 hours after TRH injection. Three reported greater engorgement of the right breast. To relieve this, the women elected to nurse their children at least an hour prior to the next scheduled feeding.

It appeared that the post-TRH elevation of prolactin, especially in phase III of lactation, augmented the production of breast milk. The exaggerated prolactin increase after TRH was evident after weaning, as demonstrated in Fig. 3. Here prolactin was measured before and 30 minutes after suckling as well as after intravenous TRH in a female physician 6 days after delivery. She returned 21 days later, having weaned her infant 4 days prior to the test. Before the test, her breasts were soft, nontender, and nipple discharge was scant. After the TRH injection, plasma prolactin rose dramatically and 2½ hours later the breasts were grossly engorged, painful, and leaking.

The consistent rise in prolactin following the intravenous injection of TRH and the subsequent breast engorgement and letdown in all instances suggest that prolactin has a significant role to play in human mammary physiology. The in vitro synthesis of specialized milk proteins such as α-lactalbumin and casein requires prolactin

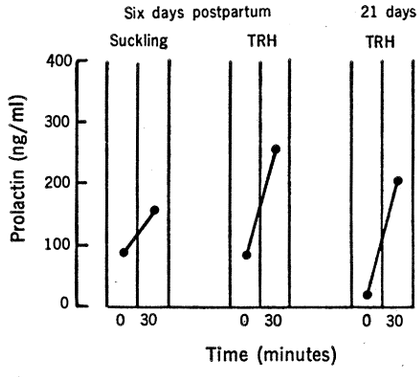

Fig. 3. Plasma prolactin before and after suckling and intravenous TRH on the sixth postpartum day (phase I) and after intravenous TRH on the 21st postpartum day (phase II) in a lactating mother.

(*6*) but the maximal effects of this unique hormone on breast tissue is seen only in the presence of insulin and hydrocortisone (*7*). The latter hormones are present in postpartum women and may promote the action of prolactin.

Postpartum, with delivery of the placenta, there is a marked reduction in estrogen and progesterone concentrations. The decrease in estrogen favors the initiation of lactation, since women receiving high doses of estrogen to suppress lactation have an increase in prolactin with suckling but fail to produce significant milk (*2*). Normally progesterone inhibits in vitro lactalbumin synthesis, hence it would seem that a reduction of both sex steroids postpartum favors milk production and the initiation of lactation. If prolactin contributes to the production of milk protein in humans, elimination of the postsuckling prolactin response in phase III should be reflected in a change in mammary milk constituents. Indeed, our preliminary observations indicate that TRH-stimulated prolactin release is followed by increases in milk fat and protein content as well as increased milk volume (*8*).

Human milk production is divided into three stages based solely upon composition (*9*). The first stage is that of colostrum (1 to 5 days). Transitional milk is present from 6 to 10 days, followed by mature human milk production thereafter. While we have been able to divide the postsuckling prolactin responses into arbitary phases, about 10 percent of lactating women respond to suckling with significant prolactin increments when studied beyond 60 days.

Ovulation in lactating women is rare before the 80th postpartum day. The anovulation appears to be the result of decreased ovarian responsiveness to circulating gondadotropins instead of a decrease in postpartum gonadotropin release (*10*). A possible relationship exists between the secretion of prolactin and the absence of ovulation in lactating women. The vaginal smear of lactating volunteers was assessed for estrogen effect. Each had an atrophic smear consisting primarily of basal and a few parabasal cells, including the woman at 410 postpartum days. While pregnancy is known to occur during lactation, the ovulatory event may be related to a decreased frequency of suckling. We are paying more attention to the frequency of suckling in an attempt to correlate this with the return of cyclic menstruation. Therefore, prolactin secretion may not only improve breast milk production quantitatively and qualitatively, but might promote a prolonged period of postpartum infertility in the nursing mother as well. In this regard the temporal association of two events may be significant and causally related, namely, when nursing fails to induce a marked increase in prolactin or when frequent suckling ceases, normal ovulatory menstrual cycles begin to return. If prolactin decreases the ovarian response to gonadotropins it may act as a natural antifertility hormone in the postpartum period. When TRH or similar hypothalamic substances which release pituitary hormones become available for oral administration, there exists the distinct possibility that breast milk production may be augmented with a concomitant prolongation of the period of postpartum infertility.

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Limit Cycles in Predator-Prey Communities

Abstract. *Essentially all models that have been proposed for predator-prey systems are shown to possess either a stable point equilibrium or a stable limit cycle. This stable limit cycle, an explicitly nonlinear feature, is commonly overlooked in conventional analyses of these models. Such a stable limit cycle provides a satisfying explanation for those animal communities in which populations are observed to oscillate in a rather reproducible periodic manner.*

The dynamics of a community comprising populations of various interacting species may, in general, be modeled by a nonlinear set of differential equations. Consequently, the equilibrium or steady-state system need not necessarily be a set of constant time-independent populations (that is, a point equilibrium such as the equilibrium of a marble in the bottom of a cup) as it must be for a linear system, but can alternatively be a stable limit cycle wherein the population numbers undergo well-defined cyclic changes in time. The amplitude of such a limit cycle, that is, the maximum and minimum values the individual populations reach during the cycle, is fixed solely by the intrinsic parameters of the model such as birth rates, predation rates, and so on. For a stable limit cycle, just as for a stable point equilibrium, the system, if disturbed, will tend to return to the equilibrium configuration. This is illustrated in Fig. 1.

In this report I consider the wide class of models which have been proposed in the ecological literature for predator-prey systems. These models, the mathematical structures of which have increasingly been guided by field and laboratory observations, incorporate a variety of forms for the stabilizing density-dependent or resource-limitation effects in the prey birth rate, and the destabilizing functional and numerical responses (*1*) on the predators' behalf (corresponding to saturation of their appetites and reproductive capacities, and like effects). Working with the full nonlinear equations, I show here that essentially all such models possess either a stable equilibrium point or a stable limit cycle.

This rather robust theorem strongly suggests that those natural ecosystems which seem to exhibit a persistent pattern of reasonably regular oscillations (*2*) are in fact stable limit cycles. This interpretation is altogether different from the widespread explanation that such phenomena are associated with the oscillations in the unrealistically special neutrally stable Lotka-Volterra system (the stability of the frictionless pendulum), where the amplitude of oscillation depends wholly on the initial conditions (on how the pendulum was set swinging).

The limit cycle is a familiar phenomenon in other areas of theoretical biology (*3*), and the Kolmogorov theorem invoked below has recently been reviewed in ecological contexts (*4*). What is new in this report is the proof that such limit cycle behavior is implicit in essentially all conventional predator-prey models.

For a community comprising one prey species and one predator species, whose populations at time t are $x(t)$ and $y(t)$, respectively, a general model for the dynamics of the system may be written

$$dx/dt = x\ g(x,y) \quad (1a)$$
$$dy/dt = y\ h(x,y) \quad (1b)$$

where g and h are some arbitrary functions of x and y. A typical example from the ecological literature (*5*) is the pair of equations

$$dx/dt = rx(1-x/K) - ky(1-e^{-\alpha x}) \quad (2a)$$
$$dy/dt = -by + \beta y\ (1 - e^{-lx}) \quad (2b)$$

The rate constants and other parameters in this particular pair of equations are as defined in (*5*) and elsewhere. The first term on the right-hand side in Eq. 2a is the prey birth rate, which includes a stabilizing density-dependent factor of the conventional logistic type. Were there no predators present, this factor would lead to a stable equilibrium point at $x = K$. Alternative expressions for the prey birth rate which are similar in effect, if different in detail, have been developed by Gompertz (*6*) [$rx \ln (K/x)$], Rosenzweig (*5*) $\{Rx^{1-a}[1-(x/K)^a]$, with $1 > a > 0\}$, and others (*7, 8*). The second term on the right in Eq. 2a represents the prey loss rate due to predation, of the form suggested on empirical grounds by Ivlev (*9*). This predation rate is proportional to x for small x, but saturates to a constant k for large x, this being a destabilizing element of the overall system. Other qualitatively similar forms have been developed by Gause (*10*) ($kx^{1/2}y$), Rosenzweig (*5*) ($kx^{\gamma}y$, with $1 > \gamma > 0$), Holling (*11*) [$kxy/(1 + cx)$], and others (*12, 13*). Similarly the second term on the right in Eq. 2b describes the relation between prey abundance and predator birth rate (Holling's numerical response), and may have either the explicit form given here or other equivalent forms (*12, 13*). The form of many of these interaction terms [particularly those in the work of Watt (*8, 12*) and Holling (*1, 11*)] is motivated by the observed properties of real predator-prey communities.

The familiar Lotka-Volterra system corresponds to the singular limiting case obtained by the use of greatly simplified forms for all terms in Eqs. 2a and 2b, namely, $K \to \infty$, $c \to 0$ with $ck =$ constant, $f \to 0$ with $f\beta =$ constant. The consequent equation has purely neutral stability. Prey and predator populations will oscillate, with their amplitudes dependent entirely on how the system started off; if disturbed, the system will oscillate with some new amplitude; and so on. This is a most fragile result, and the slightest departure from the Lotka-Volterra form, for example, K not infinite, will destroy the neutral stability property.

In systems such as those represented by Eqs. 2a and 2b there is a tension between the stabilizing resource-limitation term and the destabilizing functional and numerical response terms. In conventional analyses of such models, either by analytical (*14*) or graphical (*15*) means, the potential equilibrium populations (that is, the points where $dx/dt = dy/dt = 0$) are found first, and then the outcome of this tension between stabilizing and de-