

Reproductive Isolation Mechanism Resulting from Resolution of Intragenomic Conflict

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Submitted December 28, 1999; Accepted June 26, 2000

ABSTRACT: Crosses have revealed the species-specific, positively correlated intensities of paternally expressed growth enhancer (GE) and maternally expressed growth suppressor (GS), which serve as a reproductive isolation mechanism in many plants and animals. However, how this mechanism evolved has remained unanswered. A dynamic model shows that the conflict between paternally and maternally inherited genomes may drive them to an evolutionary "arms race" of their GE and GS productions, respectively. This results in paternally expressed GE and maternally expressed GS, and their evolutionarily stable intensities are both decreasing functions of species-specific degree of paternity and GE and GS production costs, thereby establishing a mechanism for postzygotic isolation.

Keywords: genomic imprinting, reproductive isolation, resolution of conflict, intragenomic conflict, gene coadaptation.

Genomic imprinting (i.e., gene expression depending on parent of origin; Bartolomei and Tilghman 1997; Hurst 1997; Iwasa 1998) is widely observed in mammals (Barlow et al. 1991; DeChiara et al. 1991; Haig and Westoby 1991; Zhang and Tycko 1992; Giannoukakis et al. 1993) and plants (Lin 1982; Grossniklaus et al. 1998; Scott et al. 1998). In most cases, genes with growth-enhancing effect are expressed only when passed from the father (i.e., maternally imprinted), whereas those with a countering effect as expressed only through maternal inheritance (paternally imprinted; Haig and Westoby 1991; Hurst and McVean 1997).

In both angiosperms (Nishiyama and Yabuno 1978; Johnston et al. 1980; Johnston and Hanneman 1982; Ehlenfeldt and Hanneman 1988; Haig and Westoby 1991; Katsiotis et al. 1995) and mammals (Dawson 1965) for

which genomic imprinting of growth-related factors is known, the failure of interspecific crosses caused by growth-related defects is widely observed. A general pattern in these crosses is that in one cross-developed offspring are smaller, while in a reciprocal cross-developed offspring are larger than either parent.

Moreover, in many plant species, such a breakdown of the normal development of species hybrids in either direction can be corrected by a change in the ploidy of one of the parents. This rule is known as the PNA (polar-nuclei activation) hypothesis (Nishiyama and Yabuno 1978) or the EBN (endosperm balance number) hypothesis (Johnston et al. 1980; Johnston and Hanneman 1982), which are in effect identical (Katsiotis et al. 1995) and present a simple way to predict the crossability between closely related species: to each species a specific value is assigned such that normal seed production follows from crossing between two plants whose assigned values are the same or can be made the same by modifying their ploidy levels. This rule has been reported to hold with many angiosperm species (Katsiotis et al. 1995). It suggests a species-specific balance in their correlated intensities between paternally expressed growth enhancer and its maternally expressed suppressor, which serves as a reproductive isolation mechanism (Haig and Westoby 1991).

It remains unanswered, however, how such species-specific correlative balance between paternally expressed growth enhancer and its maternally expressed suppressor may evolve. Previous models (Haig and Westoby 1989; Mochizuki et al. 1996; Haig 1997; Burt and Trivers 1998; Spencer et al. 1998) dealing separately with these imprinted factors cannot in principle provide an answer for this question. To examine this problem, we develop a model that describes the evolution of these counteracting factors.

The Model

Consider a large population in which mating is random and paternity (i.e., the probability with which randomly chosen two offspring of a mother have the same father) is p (≤ 1). Assume that offspring size r increases as growth

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enhancer (GE) production g increases, whereas it decreases as growth suppressor (GS) production s increases; for simplicity, we assume that $r = g/(1 + s)$. (With a more general form of r , $r = f[g/(1 + s)]$, where $f(v)$ is a monotone-increasing function of variable v ; we can follow the same line of logic developed here to reach the same major conclusions.) Given that each mother has a fixed amount R of resources to produce offspring, the offspring number N per mother decreases with the average offspring size \bar{r} in a mother; specifically, we adopt the most commonly used assumption (Trivers 1972; Smith and Fretwell 1974) that $N = R/\bar{r}$. Assume that the survivorship ϕ of an offspring is enhanced by an increase in its size r and that GE and GS are produced at cost of the survivorship of the offspring: $\phi(g, s) = w(r) \exp[-(c_g g + c_s s)]$, where $w(r)$ is an increasing function of r that quickly saturates with r increased (see app. A for the precise mathematical assumptions on $w(r)$), and c_g and c_s , respectively, represent the costs for unit production of GE and GS. (With alternative forms for the survivorship ϕ , such as $\phi(g, s) = w(r)/[1 + c_g g + c_s s]$ or $\phi(g, s) = w(r) - [c_g g + c_s s]$), we can follow the same line of logic developed in this article, to find the same major conclusions.)

Although some growth-related genes are known to have several pleiotropic effects (see Kornfeld 1992 for an example), for simplicity, we here assume the functions of these genes to be restricted to growth-related ones. (The case in which growth-related genes have several pleiotropic effects can be treated in this model framework by modifying the function form of r as $r = [g_0 + g]/[1 + s_0 + s]$, where g_0 and s_0 , respectively, represent the portions of GE and GS needed to be produced for other nongrowth-related functions. This modification would not change the major conclusions, as can be confirmed by following their derivation presented.)

Intragenomic Conflict

The adaptive offspring size (and GE production) for paternally (or maternally) inherited genome can be derived by examining the evolutionary dynamics under the assumption that only the genome is activated (see the legend of fig. 1 for details). As far as $p < 1$, the evolutionarily stable (Maynard Smith 1974) and also convergence stable (Christiansen 1991), production g_m^{cs} of GE for the maternally inherited genome is smaller than that for the paternally inherited genome, g_p^{cs} : $g_m^{cs} < g_p^{cs}$ (fig. 1), which implies the corresponding inequality for the evolutionarily stable offspring size: $r_m^{cs} = g_m^{cs} < r_p^{cs} = g_p^{cs}$. This discrepancy reveals a conflict over offspring size between the paternally and maternally inherited genomes, that is, an intragenomic conflict, as pointed out by Haig (1992) for the case without GE production cost (or a cost for offspring growth).

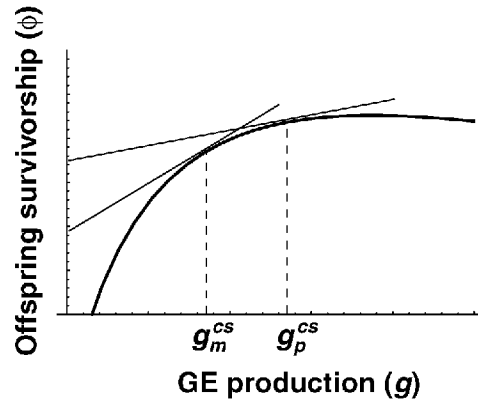


Figure 1: Conflict between the paternally and maternally inherited genomes over offspring size. In general, the shape of $\phi(g, 0) = w(r) \exp(-c_g g)$ looks like this figure because $\partial\phi(g, 0)/\partial g = [e_g w(r) - c_g w(r)] \exp(-c_g g) = w'(r)c_g [e_g/c_g - w(r)/w'(r)] \exp(-c_g g)$, and $w'(r) = 0$ for $r \leq r_0$, whereas $w'(r) > 0$, $w''(r) < 0$, and $w(r)/w'(r)$ is a monotone-increasing function of r for $r > r_0$. Suppose that only the maternally inherited genome is activated. Then, the adaptive solution for the genome would be to produce growth enhancer (GE) alone because it is not adaptive to produce two factors requiring production cost with opposite effects at the same time (to be more precise, either $\partial \ln W_m / \partial s|_{s=s} = (\partial r / \partial s)(w/w - 1/2r) - c_s$ or $\partial \ln W_m / \partial g|_{g=g} = (\partial r / \partial g)(w/w - 1/2r) - c_g$ is always negative, suggesting that either s_m or g_m must converge to 0. This is also true for s_p or g_p by the same token) and producing growth suppressor (GS) alone makes the offspring size r zero. The evolutionary change in GE production g would occur so as to increase the fitness of a maternally inherited mutant genome with GE production g' : $W_m = (1/2)\{R/(r + r'/2)\}\phi(g', 0)$, where $r = g$ and $r' = g'$ are, respectively, the wild-type and mutant offspring sizes produced by a heterozygotic (r, r') mother. Suppose now that only the paternally inherited genome is activated to the contrary. Then, by the same token, the adaptive solution would be to produce GE alone, and the evolutionary change in GE production g would occur so as to increase the fitness of a paternally inherited mutant genome with GE production g' : $W_p = (1/2)(R/[1 - (p/2)]r + (p/2)r')\phi(g', 0)$. As far as $p < 1$, the evolutionarily stable GE production g_m^{cs} for the maternally inherited genome, which satisfies $\partial W_m / \partial g'|_{g'=g} = R[2g\partial\phi(g, 0)/\partial g - \phi(g, 0)]/(2g)^2 = 0$, and thus $\partial\phi(g, 0)/\partial g = (1/2)\phi(g, 0)/g$ should locate on the left-hand side of the paternal counterpart g_p^{cs} , which satisfies $\partial W_p / \partial g'|_{g'=g} = (R/2)[\partial\phi(g, 0)/\partial g - (p/2)\phi(g, 0)]/g^2 = 0$, and thus $\partial\phi(g, 0)/\partial g = (p/2)\phi(g, 0)/g$. This implies a gap (thus, conflict) over adaptive offspring size between the paternally and maternally inherited genomes: $r_m^{cs} = g_m^{cs} < r_p^{cs} = g_p^{cs}$. In this figure, it shows the case in which $p = 0.4$, $c_g = 0.01$, $w(r)$ is given as $w(r) = 0$ for $r \leq r_0$, and $w(r) = (r - 3)/(r + 15)$.

Resolution of Intragenomic Conflict

To investigate the evolutionary consequence in a case where the maternally and paternally inherited genomes are both activated, that is, how the intragenomic conflict may be resolved (Higashi et al. 1991; Yamamura and Higashi 1992; Godfray 1995), let g_p and g_m (s_p and s_m), respectively, denote the GE (GS) production by the paternally and maternally inherited genomes. In this case,

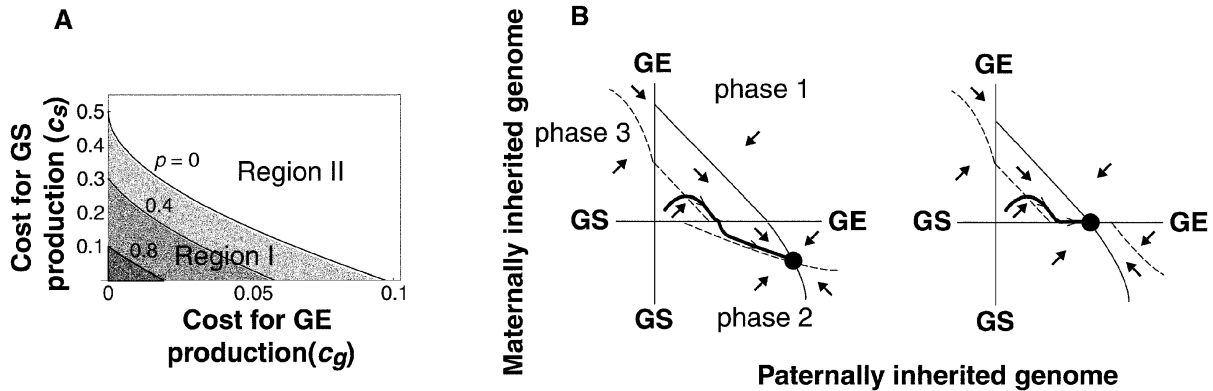


Figure 2: Coevolution of paternally and maternally inherited genomes. *A*, Two regions (regions *I* and *II*) in the parameter space (c_g, c_s) for $p = 0, 0.4$, and 0.8 that represent the conditions (derived in app. A) under which two distinctive evolutionary dynamics (shown in *B*) develop. A particular function $w(r) = (r - 1.5)/(r + 0.5)$ is used for making this figure. *B*, Evolutionary dynamics of the growth enhancer (*GE*) and growth suppressor (*GS*) productions by the maternally inherited genome (indicated by the upper half for *GE* and lower half for *GS* of the vertical axis) and those by the paternally inherited genome (indicated by the right half for *GE* and left half for *GS* of the horizontal axis) for the two cases represented by regions *I* (left panel) and region *II* (right panel) of the parameter space in *A*. The three phases, 1, 2, and 3, of the evolutionary dynamics are shown in the upper-right, lower-right, and upper-left domains, respectively, of each figure. Particular parameter values $(c_g, c_s) = (0.01, 0.03)$ and $(0.015, 0.7)$ are used for making the figures. An arrow represents the vector indicating the direction of evolutionary dynamics in each region surrounded by zero-isoclines (represented by solid lines for paternal and by dotted lines for maternal dynamics) of the dynamical system. Filled small circles represent stable steady states of the dynamical system. A typical evolutionary trajectory is indicated by a line with arrows for each of the two cases.

production level of each factor in offspring is expressed by the sum of production levels by each genome: $g = g_p + g_m$, $s = s_p + s_m$. Because it is not favored by selection to produce two costly factors with contradicting effects at the same time, the possible situations are restricted to four cases—case 1: $g_p \geq 0, g_m \geq 0, s_p = s_m = 0$; case 2: $g_p \geq 0, s_m \geq 0, s_p = g_m = 0$; case 3: $s_p \geq 0, g_m \geq 0, g_p = s_m = 0$; and case 4: $s_p \geq 0, s_m \geq 0, g_p = g_m = 0$ (see the legend of fig. 1 for a more precise reasoning). The last case is meaningless, however, in which the development of offspring does not take place at all.

The evolutionary dynamics of the *GE* and *GS* productions by the paternally and maternally inherited genomes can thus be viewed as comprised by three phases—phases 1, 2, and 3, respectively, corresponding to the above three cases 1, 2, and 3. The evolutionary dynamics in each of these phases is determined by a pair of equations:

$$\frac{d}{dt} \begin{pmatrix} X_p \\ X_m \end{pmatrix} = \begin{pmatrix} G_p & B \\ B & G_m \end{pmatrix} \begin{pmatrix} \partial \ln W_p / \partial \ln X_p |_{X_p=X_p} \\ \partial \ln W_m / \partial \ln X_m |_{X_m=X_m} \end{pmatrix}, \quad (1)$$

where (X_p, X_m) represents (g_p, g_m) for phase 1, (g_p, s_m) for phase 2, and (s_p, g_m) for phase 3; G_p and G_m are additive genetic variances for X_p and X_m , respectively; B is the additive genetic covariance between them (Lande 1981; Iwasa et al. 1991; Abrams et al. 1993); and the fitnesses W_p and W_m of paternally and maternally inherited mutant ge-

nomes X'_p and X'_m , respectively, are given appropriately for each phase (see app. A). This model assumes multiple alleles affecting the factor production. Then, it allows us to consider a continuum of expression of maternally and paternally derived alleles. (The additive genetic variances and the additive genetic covariance can change with time depending on several factors, such as mutation rate and stabilizing selection, but the results remain the same as far as B is small enough.)

The analysis of the evolutionary dynamics (app. A) identifies the two distinctive cases corresponding to regions *I* and *II* in the parameter space shown in figure 2*A*, and the system dynamics for these cases can be depicted as in figure 2*B* (left and right panels, respectively).

In the case when paternity p and the costs c_g and c_s , respectively, for *GE* and *GS* productions are high enough (to fall in region *II* of the parameter space in fig. 2*A*), at first (starting around the origin of the state space shown in fig. 2*B*), the *GE* productions g_p and g_m by maternally and paternally inherited genomes, respectively, both increase until their sum $(g_p + g_m)$ exceeds the evolutionarily stable maternal *GE* production g_m^{cs} , after which the paternal *GE* production g_p continues to grow and converges to its own evolutionarily stable intensity g_p^{cs} , while the maternal production g_m reduces to converge to 0, all within phase 1 (fig. 2*B*). As a result, the *GE* production only by paternally inherited genome (i.e., paternally expressed *GE*) evolves. This confirms Haig's conflict hypothesis on the

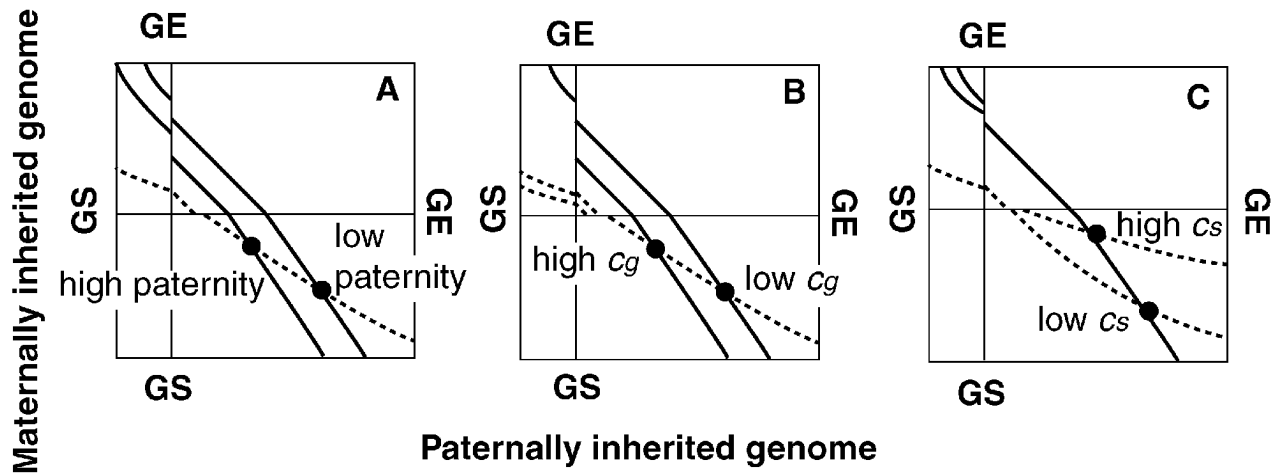


Figure 3: The dependency of paternal growth enhancer (GE) production g_p^* and the maternal growth suppressor (GS) production s_m^* on paternity p (A), the production cost c_g of GE (B) and that c_s of GS (C). Here, a particular function $w(r) = (r - 0.075)/(r + 0.75)$ is used.

evolution of genomic imprinting (Haig and Westoby 1989; Mochizuki et al. 1996; Haig 1997; fig. 2B).

In the other case (when paternity p or either of the GE and GS production costs c_g and c_s is low enough to fall in region I of the parameter space in fig. 2A), however, the system dynamics does not stop within phase 1 and moves into phase 2, in which a further drastic evolutionary development follows: an “arms race” between the GE production g_p by paternally inherited genome and the GS production s_m by maternally inherited genome (Hurst et al. 1996; McVean and Hurst 1997; Smith and Hurst 1998) develops (the left panel of fig. 2B). This arms race does not escalate infinitely but converges to an equilibrium at which each of the paternally and maternally inherited genomes cannot profit from any further factor production; thus, the conflict is resolved (Higashi et al. 1991; Yamamura and Higashi 1992; Godfray 1995). At the equilibrium, the offspring size r^* is determined between the evolutionarily stable size for the maternally inherited genome and that for the paternally inherited genome: $r_m^{cs} < r^* < r_p^{cs}$ (app. A); that is, the resolution of conflict between the paternally and maternally inherited genomes results in their compromise in offspring size.

Predictions and Supporting Evidence

It is the coevolutionary process for conflict resolution through which the paternally expressed GE (i.e., the maternally imprinted gene with offspring-enlarging effect) and maternally expressed GS (i.e., the paternally imprinted gene with the countering effect) are jointly generated. Sup-

porting evidences for this converging arms race, which leads to high production levels of paternally expressed GE and maternally expressed GS, is the finding that imprinted genes tend to have few and small introns, indicating their high transcription rates (but see Haig 1996). Hurst et al. (1996) interpreted the same finding as to falsify an “endless” arms race because introns are not completely lost; this interpretation does not contradict, but is supplemented by, our result.

The paternal GE production g_p^* ($>g_p^{cs}$) and the maternal GS production s_m^* attained at the equilibrium are functions of paternity p and GE and GS production costs c_g and c_s (app. A), which are expected to be species specific and would jointly increase with a decrease in any of these parameters: p , c_g , and c_s (app. B), as shown in figure 3. This result indicates that the species-specific, positively correlated intensities of paternally expressed GE and maternally expressed GS, which serves as a reproductive isolation mechanism, may be generated through the coevolutionary process for conflict resolution between the paternally and maternally inherited genomes over offspring size when paternity or either of the production costs of these factors is low enough. In the context of speciation, this implies that if any difference exists between two isolated populations of a species in degree of paternity or either of GE and GS production costs, it may lead to their difference in the intensities of paternally expressed GE and maternally expressed GS, as a result of the coevolutionary process of conflict resolution. The latter difference between the two populations should in turn prevent a normal de-

velopment of offspring resulted from their cross, thus establishing their postzygotic isolation.

Cross experiments provide a unique opportunity for testing the hypothesis, implied by the above result, that in a cross between two species with different degree of paternity, GE or GS production cost, the resulting offspring are larger (or smaller) than the parents when the father (or mother) is from the species of lower paternity, GE or GS production cost. Indeed, a cross between nearly monogamous and polyandrous rodent species (Dawson 1965) with growth-related imprinted genes (Vrana et al. 1998) produces offspring larger (smaller) than its parents when the father (or mother) is from the species of lower paternity, supporting the former half of the hypothesis. The latter half, requiring data on GE and GS production costs, remains to be tested.

Finally, our model predicts that the paternally expressed GE is more common than maternally expressed GS; the former evolves as long as paternity is less than (i.e., not equal to) 1 while there is a threshold in paternity beyond which the latter may evolve, given GE and GS production costs. It is difficult to test this prediction since actual functions and imprinting patterns of most imprinted genes are more complex and are not well known. However, this hypothesis might explain the observation (Barlow et al. 1991; DeChiara et al. 1991; Giannoukakis et al. 1993; Kalscheuer et al. 1993) that *Igf2* or *IGF2*, a gene coding for growth enhancer, is imprinted both in mouse and human, while *Igf2r* or *IGF2R*, coding for its suppressor (Lau et al. 1994), is imprinted only in the former because paternity is lower in mouse than in human (see Burt and Trivers 1998 for an alternative explanation). *IGF2R* in humans is biallelically expressed rather than has zero expression. This can be explained by pleiotropic effects of *IGF2R*, where a level of *IGF2R* expression is needed for other nongrowth-related functions.

Acknowledgments

We thank J. N. Thompson and N. Yamamura for comments and suggestions. The manuscript benefited from comments by N. Barton and two anonymous reviewers.

APPENDIX A

The Analysis of the Evolutionary Dynamics

The analysis of the evolutionary dynamics governed by equation (1) follows. We here assume that $B = 0$, which would not change steady states and well approximates the dynamics as long as the actual value of B is small

enough. Also, assume that $w(r)$ is a function of r such that $w(r) = 0$ for $r \leq r_0$, and $w(r) > 0$, $w'(r) > 0$, $w''(r) < 0$, and $Q(r)/r$ increases with r increased, where $Q(r) = w(r)/w'(r)$ for $r > r_0$ and further that $Q(r)/r \rightarrow \infty$ as $r \rightarrow \infty$. The assumption that $Q(r)/r \rightarrow \infty$ as $r \rightarrow \infty$ implies that $w(r)/w'(r)$ goes to infinity as $r \rightarrow \infty$ in an order greater than r . Thus, $w'(r)$ goes to 0, that is, $w(r)$ saturates, as $r \rightarrow \infty$. The assumption that $Q(r)/r$ increases with r increased implies that $w(r)$ quickly saturates as r increases. We consider below each of the three phases of the dynamics.

Phase 1: The (g_m, g_p) Coevolution

Setting the right-hand sides of equations (1) to 0, the zero-isoclines for the dynamics of g_m and g_p are, respectively, given as

$$2(g_m + g_p) \frac{\partial \phi(g_m + g_p, 0)}{\partial (g_m + g_p)} - \phi(g_m + g_p, 0) = 0, \quad (\text{A1a})$$

$$2(g_m + g_p) \frac{\partial \phi(g_m + g_p, 0)}{\partial (g_m + g_p)} - p\phi(g_m + g_p, 0) = 0. \quad (\text{A1b})$$

Note that the $(g_m + g_p)$ values that satisfy (A1a) and (A1b) equal g_m^{cs} and g_p^{cs} , respectively. Thus, equations (A1a) and (A1b) are simplified as $g_m + g_p = g_m^{cs}$ and $g_m + g_p = g_p^{cs}$, respectively, and it is clear from figure 1 that the vector field indicating the directions of the dynamics is given as in the upper-right domain of each panel of figure 2B.

Phase 2: The (s_m, g_p) Coevolution

The fitnesses in this phase are given as

$$W_m = \frac{1}{2} \left[\frac{R}{(r' + r)/2} \right] \phi(g_p, s'_m), \quad (\text{A2a})$$

$$W_p = \frac{1}{2} \left[\frac{R}{(p/2)r' + [1 - (p/2)]r} \right] \phi(g'_p, s_m), \quad (\text{A2b})$$

where

$$r = \frac{g_p}{1 + s_m}. \quad (\text{A2c})$$

Thus, setting the right-hand sides of equations (1) to 0, the zero-isoclines for the dynamics of s_m and g_p are, respectively, given as

$$2r \left[w'(r) \frac{\partial r}{\partial s_m} - wc_s \right] - w \frac{\partial r}{\partial s_m} = 0, \quad (A3a)$$

$$2r \left[w'(r) \frac{\partial r}{\partial g_p} - wc_g \right] - pw \frac{\partial r}{\partial g_p} = 0. \quad (A3b)$$

Equation (A3a), which can be rewritten as $Q(r)/r = 1/[1/2 - c_s(1 + s_m)]$, has a unique solution r (thus, $g_p > 0$) for a given s_m (≥ 0), when $c_s < (1/2)/(1 + s_m)$ (because $Q(0) = 0$ and $Q(r)/r \rightarrow \infty$ as $r \rightarrow \infty$) and the solution r (thus, g_p) increases with increased s_m . Thus, if and only if $c_s < 1/2$, the zero-isocline for the dynamics of s_m intersects with the line $s_m = 0$ at $g_p = g_p^0$ (> 0), where $r_p^0 \equiv g_p^0$ is the solution of $Q(r)/r = 1/[1/2 - c_s]$ and decreases with decreased c_s . The zero-isocline for the dynamics of g_p , given by (A3b), which can be rewritten as $Q(r)/r = 1/[p/2 + c_g g_p]$, intersects with the line $s_m = 0$ at $g_p = g_p^{cs}$, where $r_p^{cs} = e_g g_p^{cs}$ is the solution of (A3b) with $s_m = 0$, that increases with decreased c_g .

The two zero-isoclines intersect with each other if $g_m^0 < g_p^{cs}$ (the left panel of fig. 2B), whereas they do not if $g_m^0 > g_p^{cs}$ (the right panel of fig. 2B), and the vector field indicating the directions of the dynamics becomes as shown in the lower-right domain of each panel of figure 2B. The condition $g_p^0 < g_p^{cs}$ (i.e., $r_p^0 \equiv e_g g_p^0 < e_g g_p^{cs} = r_p^{cs}$) for the former case (i.e., for a coevolutionary arms race to take place) holds if and only if the point (c_s, c_g) is below a line specified by p (i.e., in region I of the parameter space) as shown in figure 2A. In this case, the intersection (g_p^*, s_m^*) , where $g_p^*, s_m^* > 0$ and the corresponding offspring size r^* (> 0) are derived as follows: it follows from equations (A2c), (A3a), and (A3b) that

$$Q(r) = 2 \left[r + \frac{(1-p)c_s r}{c_g r + pc_s} \right], \quad (A4)$$

which determines r^* as its unique solution, and that

$$g_p^* = \left[\frac{r^*}{Q(r^*)} - \frac{p}{2} \right] \frac{1}{c_g}, \quad (A5a)$$

$$s_m^* = \left[\frac{1}{2} - \frac{r^*}{Q(r^*)} \right] \frac{1}{c_s} - 1. \quad (A5b)$$

Here, we prove the relation $r_m^{cs} < r^* < r_p^{cs}$: first, g_m^{cs} is the solution of $\partial W_m / \partial g' |_{g'=g} = 0$, which can be written in terms of $Q(r)$ as $Q(r) = 2r/(2rc_g + 1)$. Thus, $r_m^{cs} = g_m^{cs}$ is the solution of this equation of r . On the other hand, r^* is the solution of (A4). Hence, we have $r_m^{cs} \leq r^*$. Next, because $g_p^* > 0$, it follows from (A5b) that $Q(r^*) -$

$1/[c_g + (p/2)r^*] < 0$. On the other hand, $r_p^{cs} = g_p^{cs}$ is the solution of $Q(r) = 1/[c_g + (p/2r)] = 0$, that is, $Q(r_p^{cs}) - 1/[c_g + (p/2r_p^{cs})] = 0$. Noting that $Q(r) - 1/[c_g + (p/2r)] = r\{Q(r)/r - 1/[c_g r + (p/2)]\}$ is an increasing function of r , it follows that $r^* \leq r_p^{cs}$.

We now prove the relation $g_p^{cs} < g_p^*$ because $r^* < r_p^{cs}$ and $Q(r)/r$ increases with r increased, we have $[r_p^{cs}/Q(r_p^{cs})] < [r^*/Q(r^*)]$. Hence, from (A5b), we have $g_p^* = [r^*/Q(r^*)] - (p/2)(1/c_g) > [r_p^{cs}/Q(r_p^{cs})] - (p/2)(1/c_g) = r_p^{cs} = g_p^{cs}$ because $Q(r_p^{cs}) = 1/[c_g + (p/2r_p^{cs})]$.

Phase 3: The (g_m, s_p) Coevolution

The fitnesses in this phase are given as

$$W_m = \frac{1}{2} \left[\frac{R}{(r + r')/2} \right] \phi(g'_m, s'_p), \quad (A6a)$$

$$W_p = \frac{1}{2} \frac{R}{(p/2)r' + [1 - (p/2)]r} \phi(g'_m, s'_p), \quad (A6b)$$

where $r = g_m/(1 + s_p)$. Thus, setting the right-hand sides of equation (1) to 0, the zero-isoclines for the dynamics of g_m and s_p are, respectively, given as

$$2r \left[w'(r) \frac{\partial r}{\partial g_m} - wc_s \right] - w \frac{\partial r}{\partial g_m} = 0, \quad (A7a)$$

$$2r \left[w'(r) \frac{\partial r}{\partial s_p} - wc_g \right] - pw \frac{\partial r}{\partial s_p} = 0. \quad (A7b)$$

Equation (A7a), which can be rewritten as $Q(r)/r = 1/(1/2 + c_g g_p)$, intersects with the line $s_p = 0$ at $g_m = g_m^{cs}$, where g_m^{cs} is the solution of (A7a) with $s_p = 0$. The zero-isocline for the dynamics of s_p , given by (A7b), which can be rewritten as $Q(r)/r = 1/[p/2 - (1 + s_p)c_s]$, intersects with the line $s_p = 0$ at $g_m = g_m^0$ (> 0), where $r_m^0 \equiv g_m^0$ is the solution of $Q(r)/r = 1/(p/2 - c_s)$ if and only if $c_s < p/2$. Noting that $Q(r_p^{cs})/r_p^{cs} = 1/(p/2 + c_g r_p^{cs})$, where $r_p^{cs} \equiv g_p^{cs}$, it follows that $g_m^0 > g_p^{cs}$. The two zero-isoclines do not intersect with each other. A proof follows. Suppose that the two zero-isoclines do not intersect with each other. Then, it holds that $Q(r)/r = 1/(1/2 + c_g g_p) = 1/(p/2 - c_s)$, which has a solution $g_p = (p - 1)/\{2[c_g + (c_s/r)]\}$, implying that $g_p \leq 0$ because $p \leq 1$. This contradicts the condition $g_p > 0$. Thus, the two zero-isoclines should not intersect with each other. The vector field indicating the directions of the dynamics are thus given as in figure 2B.

APPENDIX B

The Analysis of the Dependence of Equilibrium State on Parameters

First, we analyze the dependence of r^* on c_s , c_g , and p . The solution of equation (A4) is r^* , which is rewritten as $X(r^*)/r^* = 2\{1 + [c_s(1-p)/(c_g r^* + p c_s)]\}$. The left-hand side of this equation is an increasing function of r^* and the right-hand side is a decreasing function of r^* . Noting that the right-hand side of this equation increases with increasing c_s and with decreasing c_g and p , it follows that r^* increases with increasing c_s and decreases with increasing c_g and p .

We prove that g_p^* and s_m^* increase with decreasing c_s . Equation (A5b) implies that g_p^* is a decreasing function of c_s because $Q(r^*)/r^*$ is an increasing function of r^* that increases with increasing c_s . Equations (A2c) and (A5b) taken together give $s_m^* = r^*/g_p^* = (1/r^* c_g)[r^*/Q(r^*) - p/2]$, which imply that s_m^* decreases with increasing c_s because $Q(r^*)/r^*$ and r^* increases with increasing c_s .

Next, we prove that g_p^* and s_m^* increase with decreasing c_g . Equation (A5b) implies that s_m^* is a decreasing function of c_g because $Q(r^*)/r^*$ is an increasing function of r^* that decreases with increasing c_g . Equations (A2c) and (A5b) taken together give $g_p^* = r^*(1 + s_m^*) = (r^*/c_s)[1/2 - r^*Q(r^*)]$, which imply that s_m^* decreases with increasing c_g because $Q(r^*)/r^*$ and r^* decreases with increasing c_g . By the same token, g_p^* and s_m^* increase with decreasing p because $Q(r^*)/r^*$ is an increasing function of r^* that decreases with increasing p .

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