One and two-locus population models with differential viability between sexes: parallels between haploid parental selection and genomic imprinting

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Abstract

A model of genomic imprinting with complete inactivation of the imprinted allele is shown to be formally equivalent to the haploid model of parental selection. When single-locus dynamic are considered, an internal equilibrium is only possible if selection acts in the opposite directions in males and females. I study a two-locus version of the latter model, in which maternal and paternal effects are attributed to the single alleles at two different loci. A necessary condition for the allele frequency equilibria to remain on the linkage equilibrium surface is the multiplicative interaction between maternal and paternal fitness parameters. In this case the equilibrium dynamics are independent at both loci and results from the single-locus model apply. When fitness parameters are additive, analytic treatment was not possible but numerical simulations revealed that stable polymorphism characterized by association between loci is possible only in several special cases in which maternal and paternal fitness contributions are precisely balanced. As in the single-locus case, antagonistic selection in males and females is a necessary condition for the maintenance of polymorphism. I also show that the above 2-locus
results of parental selection model are very sensitive to the inclusion of weak directional selection on the individual’s own genotypes.

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**Running head:** parental selection
INTRODUCTION

Parental genetic effects refer to the influence of the mother’s and father’s genotypes on the phenotypes of their offspring, not attributable just to the transfer of genes. Examples have been documented across a wide range of areas of the organism biology; see, for example, Table 1 in WADE (1998) and Tables 1 and 2 in RASANEN and KRUUK (2007). Parental selection is a more formal concept used in theoretical modeling and concerns situations where the fitness of the offspring depends, besides other factors, on the genotypes of its parent(s) (generalizing from KIRKPATRICK and LANDE 1989).

Another well-known parent-of-origin phenomenon is genomic imprinting. Here, the level of expression of one of the alleles depends on which parent it is inherited from. Often it is difficult to tell apart the phenotypic patterns due to parental effects and genomic imprinting, and thus a problem arises in the process of identifying the candidate genes for such effects (HAGER et al. 2008). Analytic methods (HAGER et al. 2008; SANTURE and SPENCER 2006; WEINBERG et al. 1998) have been developed to quantify subtle differences between the two. In this article, I point out that a simple mathematical model, first suggested for genomic imprinting at a diploid locus, can be interpreted, without any formal changes, to describe parental selection on haploids.

While there has been much progress in understanding the evolution of genomic imprinting (HUNTER 2007), including advances in modeling (SPENCER 2000; SPENCER
2008), the population genetics theory of parental effects received less attention. Existing major-locus effect models of parental selection are single-locus, two-allele, and mostly concern uniparental (maternal) selection (Gavrilets and Rice 2006; Santure and Spencer 2006; Spencer 2003; Wright 1969), with only one specific case where the fitness effects of both parents interact studied by Gavrilets (1998). No attempt to extend this theory into multilocus systems has yet been made. Considering a two-locus model with both parents playing role in selection on the offspring is called for by the observation that many maternal and paternal effects aim at the different traits or different life stages of their progeny. Among birds, for example, body condition soon after hatching is largely determined by the mother, while paternally transmitted sexual display traits develop much later in life (Price 1998). Such effects are therefore unlikely to be regulated within a single locus. Sometimes the effects are on the same trait, but still attributed to different loci: expression of gene $A^{VY}$ that causes “agouti” phenotype (yellow fur coat and obesity) in mice is enhanced by maternal epigenetic modification (Morgan et al. 1999), while paternal mutations at the other locus, $MommeD4$, contribute to reverse phenotypic pattern in the offspring (Chong et al. 2007). Epigenetic state of murine $Axin^{Fu}$ allele is both maternally and paternally inherited (Rakyan et al. 2003).

Focusing selection on haploids reduces the number of genotypes that need to be taken into account, while preserving the main properties of the multilocus system. Genes with haploid expression and a potential of parental effects can be found in two major taxonomic kingdoms. A notable candidate is $Spam1$ in mice, which is expressed during sperogenesis and encodes a factor that enables sperm to penetrate the egg cumulus
This gene remains a target for effectively haploid selection, because its product is not shared via cytoplasm bridges between developing spermatides. Mutations at Spam1 alter performance of the male gametes that carry it, and might indirectly, perhaps by altering the timing of fertilization, affect the fitness of the zygote. The highest estimated number of the mouse genes expressed in the male gametes is currently 2375 (Joseph and Kirkpatrick 2004), and one might expect some of them to have similar paternal effects. Plants go through a profound haploid stage in their life cycles, and genes involved at this stage have an inevitable effect on the fitness of the future generations. In angiosperms, seed development is known to be controlled by both maternal (Chaudhury and Berger 2001; Yadegari and Drews 2004) and paternal (Nowack et al. 2006) effect genes, expressed, respectively, in female and male gametophytes.

Under haploid selection, there can be no overdominance, and thus polymorphism is much more difficult to maintain than in diploid selection models (summarized in Feldman 1971). Nevertheless, differential or antagonistic selection between sexes can lead to a new class of stable internal equilibria in the diploid systems (Bodmer 1965; Kidwell et al. 1977; Mandel 1971; Owen 1953; Reed 2007), and I make use of this property in the haploid models developed below. In the experiment by Chippindale and colleagues (Chippindale et al. 2001), approximately 75% of the total fitness variation in the adult stage of D. melanogaster was negatively correlated between males and females, which suggests that a substantial portion of the fruit-fly expressed genome is under sexually antagonistic selection. I assume that the effect of either parent on the fitness of the
individual depends on the sex of the latter, which in respect to modeling is equivalent to
the assumption of differential viability between the sexes in the progeny of the same
parent(s). Biological systems that satisfy the latter assumptions can be found among
colonial green algae: many members of the order Volvocales are haploid except for the
short zygotic stage, and during sexual reproduction, they are also dioecious and
anisogametic. I will return to this example in the DISCUSSION. A possibility that genes
expressed in animal gametes may be under antagonistic selection between sexes has been
discussed (BERNASCONI et al. 2004). For example, a (hypothetical) mutation increasing
the ATP production in mitochondria would be beneficial in sperm, because of the
increased mobility of the latter, but neutral or detrimental in the egg, due to a higher level
of oxidative damage to DNA (ZEH and ZEH 2007).

My main purpose was to derive conditions for existence and stability of the internal
equilibria of the model(s). I begin with a simple one-locus case, which can be analyzed
explicitly, and show how these one-locus results can be extended to the case of two
recombining loci with multiplicative fitness. Then, I assume an additive relation between
the maternal and paternal effect parameters and study the special cases where parental
effects are symmetric.

ONE LOCUS

Model 0 – Haploid viability selection: I first examine a standard haploid single-locus
diallelic model with viability (gametic) selection (BÜRGER 2000). Constant selection
pressure, random mating, unlimited population size and discrete generations are assumed. When there are no differences between sexes, the fitter of the two gametes, $A$ or $a$, eventually gets fixed and no polymorphic equilibrium is possible. Let us examine a special case where viabilities of the gamete $A$ differ between males and females, and the viabilities of the gamete $a$ equal 1 regardless of sex. The frequency $p'_i$ of $A$ in the sex $i$ ($i = m$ for males and $i = f$ for females), after meiosis and selection, is:

$$p'_i = \frac{w_{A,i}(p_m + p_f)}{2 - (1 - w_{A,i})p_m - (1 - w_{A,i})p_f},$$

where $p_m$ and $p_f$ are the pre-selection frequencies of $A$ in males and females, respectively, and $w_{A,i}$ is the fitness of $A$ in sex $i$. Let $w_{A,m} = 1 - \alpha$ and $w_{A,f} = 1 - \delta$, for males and females, respectively. A single polymorphic equilibrium is given by:

$$p_m = \frac{(1 - \alpha)(\alpha + \delta)}{(\delta - \alpha)\alpha}; \quad p_f = \frac{(1 - \delta)(\alpha + \delta)}{(\alpha - \delta)\delta};$$

(1)

The equilibrium (1) exists, and is stable, if and only if

$$-\delta > \alpha > \frac{\delta}{2\delta - 1};$$

(2)
Reversing left and right parts of the inequality (2) gives the conditions for stability of fixations at $p_{m,f} = 0$, $p_{m,f} = 1$, respectively*.

**Model 1 – parental selection / imprinting:** In this model, the fitness of the haploid individual depends on the genotype of its haploid parent, but not on its own genotype. An allele $A$ is assumed to have an effect on the offspring fitness, when it is found in only one of the parents (assumed to be a father in the following), whereas an $a$ allele has no effect. This model is mathematically equivalent to the model of maternal imprinting with complete inactivation of the imprinted allele (ANDERSON and SPENCER 1999; PEARCE and SPENCER 1992). Since in the latter model individuals are functionally haploid at the imprinted locus, their viabilities depend on the genotype of the paternal gamete, which in terms of the parental selection model is equivalent to a haploid father (Table 1). When sex is irrelevant to selection, both models have the same dynamics as Model 0 (as pointed out by PEARCE and SPENCER 1992), with selection acting on paternal gametes only. When individual fitness depends on sex, the imprinting model is not formally equivalent to any other two-sex viability or fertility model, but it remains equivalent to the parental selection model. Its dynamics have been examined by ANDERSON and SPENCER (1999). I repeat their results here, using the interpretation of parental selection. Let the paternal frequencies $A$ and $a$ alleles be $p_m$ and $q_m = 1 - p_m$, respectively; and $p_f$ and $q_f = 1 - p_f$ be the maternal frequencies of the same alleles. As before, when equations are

* Analyses of stability of all gene frequency equilibria presented in this paper were done by examining the Jacobian matrix of partial derivatives at the equilibrium point, unless stated otherwise. Details are available as an electronic supplement (Mathematica 5.2 notebook) from http://www…
the same in both sexes, a subscript $i$ is used in the gene frequency and fitness notations to indicate sex ($i = m$ for males and $i = f$ for females). Let the fitnesses of the progeny of a father of genotype $A$ be $w_i$, and since $a$ was postulated to have no parental effect, it is reasonably to assume that the fitness of the offspring from this paternal genotype is 1. At the next generation:

$$p_i' = \frac{1}{2} \left( p_f q_m + w_i p_m \left(1 + p_f\right) \right) \left( w_i p_m + q_m \right)$$  \hspace{1cm} i = m, f \; ; \hspace{1cm} (3)$$

If written down for $q_m'$ and $q_f'$, and with appropriate change in the fitness notations, eq (3) is identical to (1) in Anderson and Spencer (1999). Let $w_m = 1 - \alpha$ and $w_f = 1 - \delta$.

Two fixation and one internal equilibria are possible, the latter taking the form:

$$p_m = \frac{\alpha + \delta}{2\alpha\delta} ;$$ \hspace{1cm} (4a)

$$p_f = \frac{(1 - \delta)(\alpha + \delta)}{\delta(\alpha - \delta)} ;$$ \hspace{1cm} (4b)

As Anderson and Spencer (1999) have shown, conditions for existence and stability of the equilibrium (4) are identical to those derived by Bodmer (1965) for his model of differential fertility / viability between sexes (also see Gavrilets and Rice 2006, p. 3033) and by Cooper (1976) for his model of X-inactivation system in marsupials.

Comparison with the results from the previous section reveals that they are also exactly the same as conditions (2) in the Model 0 of haploid viability selection. As will be shown
later on, there are cases where the same or very similar sets of inequalities define existence and stability of the polymorphic equilibria in the two-locus model.

TWO LOCI

**Model 2 – maternal and paternal selection:** This model is a two-locus extension of the Model 1. As before, the allele $A$ at the locus $A/a$ is assumed to have a paternal effect on the offspring fitness. An allele $B$ with the frequency $u$ at the second locus, $B/b$, is assumed to alter the offspring fitness only when it is found in the mother, i.e. it has a *maternal* effect, while an allele $b$ with the frequency $v = 1 - u$ has no effect. The offspring fitness is therefore dependent on the genotypes of both parents; I will say that those resulting from the mating between $A$ father and $B$ mother experience *joint* parental effect, while those from the union of $a$ father and $b$ mother have received *none* effect.

The offspring phenotypes are thus divided in four groups (*paternal, maternal, none* and *joint* parental effects), and the subscript $\phi$, ranging from 1 to 4, respectively, added to the genotypic frequency notation, will denote the frequency of this genotype within the corresponding phenotypic group. Proportions of the mating types resulting in different genotypes/phenotypes are given in Table 2; the frequency of a particular type after meiosis is obtained by summing the products of the corresponding male and female parental frequencies, multiplied by the factors from respective table entries. The following recursion can be drawn:

$$
\bar{w}_i P_i(x) = \sum_{\phi=1}^{4} P(x)\phi w_{i,\phi} \quad i = m, f;
$$

(5)
where \( P(x) \) is the frequency of a genotype \( x \), i.e. \( AB, Ab, aB \) or \( ab \); within the phenotypic group \( \phi \) (ranging from 1 to 4), before selection. \( P(x)' \) is the frequency of \( x \) in sex \( i \), after sex-specific selection. \( w_{i,\phi} \) is the fitness of the phenotype \( \phi \) in sex \( i \), and \( \bar{w}_i \) is the mean fitness of this sex. \( \bar{w}_i \) can be conveniently expressed in terms of allele frequencies, by noting that the frequencies of offspring phenotypes are simply the outer products of the allele frequencies at paternal effect locus in males and maternal effect locus in females. Following selection, we have:

\[
\bar{w}_i \cdot P(x)' = M_{ik} w_{i,\phi} \quad \quad i = m, f; \quad k = \phi = 1, 2, 3, 4; \quad (6)
\]

where \( M_k \) is the corresponding (with subscript \( k = \phi \) ranging from 1st to 4th) element of the frequency of the offspring phenotype \( \phi \) in sex \( i \). The mean fitness, \( \bar{w}_i \), is therefore:

\[
\bar{w}_i = \sum_{\phi=1}^{4} M_{ik} w_{i,\phi} \quad \quad i = m, f; \quad k = \phi = 1, 2, 3, 4; \quad (7)
\]

To adequately link the allele and genotype frequencies, two measures of disequilibria between loci, \( D_m \) and \( D_f \), among males and females, respectively, need to be included (Table 3). Note from Tables 1 and 2 that genotype frequencies now depend on the recombination rate between loci, \( r \).
It is easy to see that Model 2 applies to both parental selection and genomic imprinting just as Model 1 does so. The former model might be interpreted such as that locus $A/a$ is maternally inactivated, while locus $B/b$ is silenced paternally. Fitness parameters therefore correspond to individual alleles, and selection acts on the genotypically diploid, but functionally haploid individuals. To avoid confusion, the results of the Model 2 will be presented using the terms of parental selection, but the fact that they can have dual biological interpretation must be kept in mind.

**Polymorphism is maintained at linkage equilibrium ($D = 0$) under multiplicative fitness:** Let us first examine a simplified case where loci are unlinked ($r = \frac{1}{2}$), and population is at linkage equilibrium ($D_m, D_f = 0$). It is easily shown (Appendix A) that in the next generation, linkage equilibrium is maintained ($D'_m, D'_f = 0$), if and only if:

$$w_{i,1}w_{i,2} = w_{i,3}w_{i,4} \quad i = m, f \quad ;$$

(8)

That is, in absence of the physical linkage between loci, population remains at linkage equilibrium, if, and only if, for both male and female offspring, the fitness product of the individuals provided with only paternal and only maternal effect is equal to the fitness product of the individuals provided with neither effect and with the joint effect of both parents. Note that for $r \neq \frac{1}{2}$, $D'_m, D'_f$ can be non-zero for a range of allele frequencies and fitness parameters (eq (2) in the Appendix A). Equation (8) is analogous to those defining multiplicative non-epistasis in the standard two-locus viability selection models.
(Karlin 1975). Let us now assume, as in Model 1, that the fitness of individuals not experiencing any (none) parental effect(s) is $w_{i,3} = 1$. The modified condition (8),

$$w_{i,4} = w_{i,1}w_{i,2},$$

will set limits of a special multiplicative fitness case in the parental selection model. Now relax the initial assumptions of $r = \frac{1}{2}$ and $D = 0$, and substitute $w_{i,4}$ with $w_{i,1}w_{i,2}$ in the general recursions (5). The resulting dynamical system has a single polymorphic equilibrium at $D = 0$, where the allele frequencies at maternal and paternal effect loci are independent of each other. That is: (i) multiplicative fitness ensures that any association between loci is eventually eliminated from the population as the allele frequency equilibrium is approached, and (ii) the frequencies $p_m$ and $p_f$ of $A$ allele at equilibrium are determined solely by the fitness parameters $w_{m,1}$ and $w_{f,1}$, i.e. by paternal effect on the fitness of males and females, but not by maternal effect parameters $w_{m,2}$ and $w_{f,2}$; analogously, equilibrium dynamics at $B/b$ locus depends only on $w_{m,2}$ and $w_{f,2}$ but not on $w_{m,1}$ and $w_{f,1}$. The internal equilibria at each locus are (independently) described by the eq (4), and condition for their existence and stability by eq (2), as in the single-locus Model 1. Note, that stability conditions of equilibria in the multiplicative case are also independent of the recombination rate $r$ (see Appendix A).

Additive fitness – general case: An alternative to the assumption that parental selection acts multiplicatively is to assume that maternal and paternal effects are added when provided to the same individual. The resulting fitness scheme is different, however, from the additive non-epistasis sensu Karlin (1975), because I make no assumption about the parental effects of the alternative alleles $a$ and $b$, but simply leave the phenotypes not
experiencing any (none) effect with the fitness = 1. Fitnesses of the parentally induced phenotypes are hereby divided into two additive components, one of which is the constant = 1, and the second is the actual contribution from parental effect(s). This approach is reflected in the following fitness matrix:

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>paternal ($w_1$)</th>
<th>maternal ($w_2$)</th>
<th>none ($w_3$)</th>
<th>joint ($w_4$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males ($w_m$)</td>
<td>$1 - \alpha$</td>
<td>$1 - \beta$</td>
<td>1</td>
<td>$1 - \alpha - \beta$</td>
</tr>
<tr>
<td>Females ($w_f$)</td>
<td>$1 - \delta$</td>
<td>$1 - \gamma$</td>
<td>1</td>
<td>$1 - \delta - \gamma$</td>
</tr>
</tbody>
</table>

Unlike multiplicative fitness case in the previous section, the additive fitness case cannot be simply reduced to a one-locus system. It is useful therefore to visualize the number of possible equilibria in the genotype frequency tetrahedron (Fig. 1). The population at any time is described by two points, indicating genotype frequencies among males and females, respectively, inside the tetrahedron. The space inside the tetrahedron indicates possible 2-locus polymorphisms, the corner vertices represent fixations at both loci and the edges represent polymorphisms with one locus fixed and the other polymorphic. The equilibria at the edges have close parallels with the single-locus Model 1. For example, the equilibrium at the $AB - aB$ edge has the form:

$$p_m = \frac{(1 - \gamma)\alpha + (1 - \beta)\delta}{2\alpha\delta};$$  \hspace{1cm} (9a)
\[ p_f = \frac{(1 - \gamma - \delta)(\alpha(1 - \gamma) + \delta(1 - \beta))}{\delta(\alpha(1 - \gamma) - \delta(1 - \beta))}; \]  

(9b)

And the equilibrium at the Ab – ab edge is obtained from (9) by substituting \( \beta, \gamma \) with 0.

The resulting equations are identical to (4) that describe internal equilibrium in the single-locus case (Model 1).

**Numerical results:** Analytical treatment of the two-locus model with additive fitness is difficult due to the number of independent parameters involved. I therefore start with numerical analysis of the general additive case, while the analytic results for several special cases will be presented in the next section. A series of \( 10^5 \) iterative simulations was run with parameters \( \alpha, \delta, \beta \) and \( \gamma \) sampled uniformly from the interval \([1, -2]\), ensuring that \( \alpha + \beta \) and \( \delta + \gamma \) do not exceed 1. Fifty sets of the initial frequencies of genotypes, with neither genotype fixed, were drawn by the broken-stick method for each parameter set, with recombination rate \( r \) varying uniformly from 0 to \( \frac{1}{2} \). A series of iterations was considered to reach its equilibrium point when the computed change in the genotype frequencies was less than \( 10^{-3} \) in 1000 generations.

**2-locus polymorphism requires symmetry in fitness parameters:** Among the numerically obtained equilibria, the two-locus polymorphisms were rare: only 21 out of \( 10^5 \) parameter combinations were able to maintain intermediate frequencies at both loci. Furthermore, all these combinations were characterized by certain symmetry of parameter values, and fell into the following categories: (i) antagonistic selection between phenotypes, i.e.
$\beta = -\alpha$ and $\delta = -\gamma$; (ii) equal contributions from both parents, i.e. $\beta = \alpha$ and $\gamma = \delta$; and (iii) antagonistic selection between sexes, i.e. $\delta = -\alpha$ and $\beta = -\gamma$. Here, the approximation sign means that the difference between the corresponding parameter values used in the simulations was less than $10^{-3}$. Further analysis of the cases (i – iii) above will be presented in the next section.

**Edge equilibria (one-locus polymorphism):** Whether the edge equilibrium (4) or (9) was the outcome of the simulation appeared to be determined by a few simple inequalities. Firstly, in all runs that resulted in the equilibrium point with one locus fixed and the other retaining polymorphism, the sex-specific fitness parameters at the polymorphic locus were of opposite sign; that is, equilibrium with polymorphism at the $A/a$ locus and fixation at the $B/b$ locus required that $\alpha > 0, \delta < 0$ or $\alpha < 0, \delta > 0$; likewise, $\beta > 0, \gamma < 0$ or $\beta < 0, \gamma > 0$ was required for polymorphism at $B/b$ locus and fixation at $A/a$ locus.

Another strictly necessary, though by no means complete, condition for the equilibrium to be found at the $A b – a b$ (polymorphism at $A/a$ locus and fixation for $b$ allele) and $A B – A b$ (polymorphism at $B/b$ locus and fixation for $A$ allele) edges of the genotype frequency tetrahedron, was:

$$\alpha + \delta < \beta + \gamma; \quad (10a)$$

That is, when paternally induced phenotypes were under weaker selection than maternally induced ones, the frequency of $A$ allele in the edge equilibrium was always higher than the frequency of $B$ allele. Likewise, fixation at the $A B – a B$ (polymorphism at
A/a locus and fixation for B allele) and aB–ab (polymorphism at B/b locus and fixation for a allele) edges of the genotype frequency tetrahedron was possible only if:

\[ \alpha + \delta > \beta + \gamma; \]  

That is, a maternal effect weaker relative to the paternal one always resulted in the higher frequency of B allele at the edge equilibrium.

**Analytical results – special cases:** The following simplifications (i – iv) of the additive fitness case allowed the analysis of existence and stability of fixation and polymorphic equilibria. Specifically, the cases (i-iii) correspond to the three combinations of parameter values for which the numerical simulations suggested occurrence of the 2-locus polymorphism.

(i) *Antagonistic selection between phenotypes:* Let \( \beta = -\alpha \) and \( \delta = -\gamma \) in the general additive case. That is, among the affected phenotypes, the increase (decrease) in fitness due to the paternal effect is equal to the fitness loss (gain) due to the maternal effect. Analysis shows that neither fixations for the AB nor ab genotype, nor edge equilibria analogous to (4) and (9) are stable. Conditions for the stability of fixations for the Ab and aB genotypes are in fact the same as those for the corresponding fixations for A and B alleles in the one-locus case (Fig. 2). That is,

\[ p_m, p_f = 1, u_m, u_f = 0 \quad (Ab \text{ fixed}) \quad \text{is stable if} \quad \alpha > \frac{-\delta}{2\delta + 1}; \]  

(11a)
\[ p_m, p_f = 0, u_m, u_f = 1 \text{ (aB fixed) is stable if } \alpha < \frac{\delta}{2\delta - 1}; \quad (11b) \]

One can see that inequalities (11a) and (11b) are symmetrical relative to \( \alpha = -\delta \) line and the inequality (11b) is identical to the reversed right-hand part of (2) in the haploid viability Model 0 and in Model 1 of single-locus parental selection / genomic imprinting (see inequality (7) in Anderson and Spencer (1999); compare also Fig. 2 here with Fig. 1 in their paper). Recall that in the single-locus Model 1, instability of fixations means stability of the internal equilibrium. Since it can be shown that the edge equilibria are always unstable in the case above (see electronic supplement), it is worth checking whether a 2-locus polymorphism is stable in the interval of \( \frac{-\delta}{2\delta + 1} > \alpha > \frac{\delta}{2\delta - 1} \).

Repeating the numerical results from the previous section, with the parameter values forced to satisfy the above inequality, demonstrates that the 2-locus polymorphism is always stable, though no analytical treatment is possible. In the following cases (ii –iii), conditions for stability of the 2-locus polymorphism are confirmed numerically in a similar manner.

(ii) Equality of maternal and paternal effects: Let \( \beta = \alpha \) and \( \gamma = \delta \). Also let the fitnesses of phenotypes affected by both parents be \( 1 - t\alpha \) and \( 1 - t\delta \), for males and females, respectively. The resulting fitness scheme is not a variant of the general additive case, except for \( t = 2 \). The outcome of the local stability analysis depends on whether parameter \( k \) is larger or lesser than 1: if \( t > 1 \), fixations for \( Ab \) and \( aB \) genotypes are
always unstable, while conditions for stability of fixations for $AB$ and $ab$ genotypes take
the following form:

\[
p_m, p_f = 1, \ u_m, u_f = 1 \quad \text{is stable if} \quad \alpha < \frac{\delta}{2k\delta - 1}; \quad (12a)
\]

\[
p_m, p_f = 0, \ u_m, u_f = 0 \quad \text{is stable if} \quad \alpha > -\delta; \quad (12b)
\]

and the 2-locus polymorphism, as seen from the numerical explorations, appear to be
stable when both inequalities are reversed:

\[
-\delta > \alpha > \frac{\delta}{2k\delta - 1} \quad \text{(12c)}
\]

If $t < 1$, conditions (12b) and (12c) hold true, but in order for the fixation of $AB$ genotype
to be stable, inequality (12a) must be reversed. The fixation for $AB$ therefore shares
stability range with either 2-locus polymorphic equilibrium or the fixation for $ab$
genotype. The corner equilibria $Ab$ and $aB$, which were unstable for $t > 1$, can both be
simultaneously stable if $t < 1$ and if condition (12a) is satisfied (Fig. 3). As numerical
tests show, which of the corner equilibria is reached appears to be determined by the
initial frequency ratio of $A$ and $B$ alleles: genotype $Ab$ becomes fixed if \( \frac{p}{u} > 1 \), and,
respectively, $aB$ is fixed when \( \frac{p}{u} < 1 \) in the initial population. Note that this condition
holds for whatever small values of $p$ and $u$ and is independent of $\alpha$ and $\delta$. For example, a
maternal effect allele can reach fixation from small initial frequency, provided this
frequency is still higher than that of the allele with paternal effect, even if it benefits sons in the expense of daughters.

(iii) **Antagonistic selection between sexes**: Let $\delta = -\alpha$ and $\beta = -\gamma$. That is, selective advantage in males (females) brought about by the paternal (maternal) effect is precisely balanced by the fitness loss due to the same effect in the other sex. In this case, fixation at neither one nor both loci is stable, but numerical results from the previous section suggest that a 2-locus polymorphism is globally stable.

(iv) **No difference in fitness between sexes**: Let $\alpha = \delta, \beta = \gamma$, i.e. there is no difference in fitness between males and females. I have already mentioned that, without selection being sex-specific, the single locus Model 1 reduces to the haploid viability model, which has only trivial equilibria. Similar equilibrium dynamics is observed at $D = 0$ surface in the two-locus Model 2 with additive fitnesses. That is, global stability of the fixations of $A$ and/or $B$ alleles is ensured by the corresponding fitness parameter ($\delta$ and/or $\gamma$) being negative, fixations for $a$ and/or $b$ are globally stable otherwise. Away from the linkage equilibrium ($D \neq 0$), there exists a pair of feasible polymorphic equilibria, in which the frequency of one allele is conditioned by the other, the recombination rate $r$ depends on the allele frequency and $D$ is equal among males and females:

$$p = \frac{1}{2} \pm \frac{\sqrt{\delta^2 - 4u(1-u)\gamma^2}}{2\delta}; \quad (13a)$$

and
\[
 r = \frac{\gamma(1-2u) + \sqrt{\delta^2 - 4u(1-u)\gamma^2}}{\delta - \gamma - 2};
 \]

(13b)

and

\[
 D = -\frac{u(1-u)\gamma}{\delta};
 \]

(13c)

where \( p = p_m = p_f \); \( u = u_m = u_f \);

It can be seen that if \( u = 1 \) or 0 in the eqn (13a), \( p \) can too only take values of 1 and 0, which implies that (13) can not be reduced to the edge equilibrium. Although equilibria (13) can be feasible (the full conditions of existence and feasibility can be found in the electronic supplement), one eigenvalue of the system’s Jacobian at the corresponding points is always greater than unity, and thus they are never stable.

**Effect of selection on the individual’s own genotype:** It is not unlikely for alleles with parental effects to alter the individual’s own fitness (ARBEITMAN et al. 2002; SPENCER 2003). To see how sensitive the equilibria in the parental selection model are to the weak viability selection acting on the individual’s own genotype, two new parameters were included in the general model. Let \( G_1 \) and \( G_2 \) be the fitnesses of the genotypes containing \( A \) and \( B \) alleles, correspondingly, while the fitnesses of \( a \) and \( b \) alleles are set to 1. Multiplicative non-epistasis is assumed between these viability parameters (KARLIN 1975), with no difference between sexes. While it was not my purpose to analyze the complete dynamics of the resulting complex model, I could show that only a weak selection on the offspring genotypes can significantly shift the model’s equilibria from one type to another. In particular, for a parental selection parameter set that would
otherwise resulted in the corner or edge equilibrium, the 2-locus polymorphic equilibria become possible for a certain range of individual viabilities (Fig. 4).

**DISCUSSION**

A model of genomic imprinting, first proposed by PEARCE and SPENCER (1992), with complete inactivation of the imprinted allele, is mathematically equivalent to the model of parental selection on haploids. Similarity of its equilibrium behavior to the earlier models of sex-specific selection has been noted before (ANDERSON and SPENCER 1999). Only when selection acts in the opposite directions in respect to males and females, is a unique internal equilibrium possible, with the same stability conditions as in BODMER’s (1965) model of differential viability/fertility between sexes (ANDERSON and SPENCER 1999). Very similar inequalities determine stability of polymorphism in a diploid model of combined maternal selection on males and direct selection on females, with the respective parameter space reduced by dominance (GAVRILETS and RICE 2006). In this paper, I have extended PEARCE and SPENCER’s original model into a two-locus system, and shown that it has the same equilibrium dynamics as a pair of one-locus models if and only if the fitness parameters at maternal and paternal effect (or paternally and maternally imprinted) loci are multiplicative. I have obtained results that are quite different from those of a well-known diploid 2-locus viability selection theory (BÜRGER 2000; KARLIN 1975). In the latter, henceforth termed VSM (for Viability Selection Model), internal equilibria on the $D = 0$ surface exist in both multiplicative and additive fitness cases, whereas polymorphic equilibria involving associations between loci ($D \neq 0$) are only
possible in the multiplicative case, and when recombination rate is low. In contrast, the additive fitness case in the parental selection / imprinting model (PSM in the following) does not allow for a stable 2-locus polymorphism at $D = 0$ surface, but is the only case where equilibria at $D \neq 0$ were detected numerically. Away from equilibrium, in the multiplicative case of PSM, association between loci can be generated by selection, provided that there is linkage between loci ($r \neq \frac{1}{2}$, see Appendix A); whereas in the multiplicative case of VSM, linkage equilibrium, once reached, is preserved for any $r$, even when the allele frequencies are not in equilibrium (BÜRGER 2000). Conditions for existence and stability of equilibria are also not analogous: in VSM, polymorphism is ensured by heterozygote superiority at each locus, while in PSM, it is antagonistic selection between sexes that allows the polymorphic equilibria (on or away from $D = 0$ surface) to exist.

Results of the analysis of PSM generally support intuition. In order for the parental effect / non-imprinted allele to reach fixation in the multiplicative case, its average fitness effect must exceed 1, and it is the fitter of maternal and paternal effect alleles that becomes fixed or is maintained at the higher frequency in the additive case. Only in the special additive case (ii), with the fitness parameter $t < 1$, are the results somewhat counter-intuitive, admitting two simultaneously stable equilibria. Analogy of the latter condition with the dominance relation in diploid systems is apparent: previous studies on the sex-specific selection show that simultaneous existence/stability of two or more equilibria requires fitness of a heterozygote to be different from 1; in particular, there must be
overdominance in one (MÉRAT 1969) or both sexes (BODMER 1965; KIDWELL et al. 1977; OWEN 1953).

Although I have only examined the fitness effects conveyed in one direction, i.e. from a parent to its offspring, it is likely that the fitness of the former is also affected by the advance of the corresponding parental effect allele. With both maternal and paternal effects taking place, a sexual conflict might be expected to arise, particularly, when sons benefit from their father’s contribution but daughters do not so, and vice versa. For example, when males of the dung beetle Onthophagus taurus help females to provide food to the offspring, their sons inherit a specific paternal phenotype characterized by large body size and the presence of horns. Males with such phenotypes are generally more successful in securing mating, thus increasing the chances of their patrilinear genes spreading in the population (HUNTER 2007). The above theoretical study suggests that in a two-locus system, a conflict between parents is only relevant if maternal and paternal fitness effects are not multiplicative, since only with multiplicative fitnesses are the equilibria at either locus independent. Under the assumption of additive fitness, however, a hypothetical parental conflict may not be easily resolved. In fact the only stable equilibria in which maternal and paternal effect alleles can both be found at intermediate frequencies require exact balance between the respective fitness parameters and therefore are likely to be very rare. Additivity of the fitness effects is expected when a common resource, such as food, is simultaneously provided by both parents. The above interpretation is not much different when viewed in terms of genomic imprinting (to which the present results equally apply), only here the effect of a parent is mediated
through the conventional inheritance. The role of the sexual conflict in the evolution of genomic imprinting has been widely discussed before (Chapman et al. 2003; Day and Bonduriansky 2004; Moore and Haig 1991).

The formal equivalence of the genomic imprinting model with that of haploid parental selection is not surprising given the similarity of the nature of these two phenomena. A possibility that imprinted genes may have evolved from those with maternal (paternal) effect has been discussed by Chandra and Nanjundiah (1990). In context of the model presented here, an evolutionary switch from the predominantly haploid to predominantly diploid phase would serve as a driving force for a pair of the parental selection loci to start functioning as diploid counterparts with the opposite imprinting patterns. Genomic imprinting in respect to determination of the mating type is known for yeasts (Klar 1990), so discoveries supporting the above reasoning are not improbable among other lower eukaryotes with both haploid and diploid stages active. Note, however, that my model only concerns those cases in which the imprinted allele is completely inactivated.

It is not easy to find a combination of haploidy, parental and sex-specific selection in one realistic biological example. At least one system, however, possesses features that resemble all the main assumptions of the model of parental selection presented above: the colonial algae Volvox carteri reproduces asexually under normal conditions but can enter the sexual stage once its environment becomes harsh. This change is triggered by a sexual pheromone, which, even at very low concentrations, interacts with the extracellular matrix surrounding the colony and, consequently, switches on the expression of a number
of genes that are known to play role both in gametogenesis and wound-healing (AMON et al. 1998). The sex-inducing pheromone itself is a glycoprotein analogous to those composing the extracellular matrix, and thus appears to have a similar genetic background. If any mutations in this set of genes were to alter the penetrability of the sexual inducing signal, or the timing of the switch to sexual reproduction etc., they would inevitably affect the fitness of the offspring of the mutants. Since V. carteri is anisogamous and has strictly genetic mechanism of sex-determination (KIRK and NISHII 2001), it is not implausible that different mutations may have different fitness effects on the male and female colonies/gametes in the subsequent generations. There has been a recent rise of interest in V. carteri as a model organism for studying the evolutionary earliest molecular mechanisms of cell-differentiation and sexual versus asexual reproduction (ARMIN 2006; KIRK and KIRK 2004). One might reasonably expect more empirical findings relevant to the theoretical modeling of parental selection at the haploid level to be made soon.

Previous studies of the parental (maternal) selection that use a major locus effect approach (GAVRILETS and RICE 2006; SANTURE and SPENCER 2006; SPENCER 2003; WADE 1998; WRIGHT 1969) are complemented by those that use the methods of quantitative genetics (HAGER et al. 2008; KIRKPATRICK and LANDE 1989; WADE 1998). None, to my knowledge, has focused on the interaction between the effects of both parents, despite empirical evidences that both mother and father contribute to the selection pattern on their offspring (CHAPMAN et al. 2003; HUNTER 2007; RAKYAN et al. 2003). It will be interesting to discover if considering maternal and paternal effects as
quantitative traits would result in the similar predictions about the sexual conflict to those derived in the present study. Another important direction for the future research is to focus on the interaction between parental and offspring genotypes, an approach used by Gavrilets (1998) and Spencer (2003). An ease with which the parental selection model’s equilibria are changed by inclusion of the weak directional selection on the offspring’s own genotypes suggests that such interactions might have a complex nature.

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LITERATURE CITED


RAKYAN, V. K., S. CHONG, M. E. CHAMP, P. C. CUTHBERT, H. D. MORGAN *et al.*, 2003 Transgenerational inheritance of epigenetic states at the murine Axin(Fu) allele occurs after maternal and paternal transmission. Proc Natl Acad Sci U S A **100**: 2538-2543.


Appendix A

The fact that linkage equilibrium in the Model 2 can only be maintained if fitness is multiplicative can be demonstrated as follows. Assume that loci are unlinked \((r = \frac{1}{2})\), and population is currently at linkage equilibrium. After meiosis and selection, the associations between loci take the form:

\[
D_m' = \frac{1}{4} \frac{\left(w_{m,3}w_{m,4} - w_{m,1}w_{m,2}\right)p_m q_m u_f v_f}{\left(p_m \left(w_{m,1}v_f + w_{m,2}u_f\right) + q_m \left(w_{m,2}u_f + w_{m,3}v_f\right)\right)^2} \tag{A1a}
\]

\[
D_f' = \frac{1}{4} \frac{\left(w_{f,3}w_{f,4} - w_{f,1}w_{f,2}\right)p_m q_m u_f v_f}{\left(u_f \left(w_{f,2}q_m + w_{f,4}p_m\right) + v_f \left(w_{f,2}p_m + w_{f,3}q_m\right)\right)^2} \tag{A1b}
\]

Substituting \(D_m', D_f' = 0\) in (A1) returns the only solution that allows polymorphism at both loci:

\[
w_{i,1}w_{i,2} = w_{i,3}w_{i,4} \quad \quad \quad \quad i = m, f;
\]

This is equation (8) in the text. Let us now relax the assumption of free recombination between loci, holding that eq (8) is true and \(w_{i,3} = 1\). Eq (A1) will take the form:
\[
D_i' = \left( r - \frac{1}{2} \right) \frac{p_f q_m - p_m q_f w_{i,1}}{(q_m + p_m w_{i,1})(v_f + u_f w_{i,2})} \quad i = m, f;
\]

(A2)

For \( r \neq \frac{1}{2} \), \( D_i' \) in eq (A2) can be non-zero for a range of allele frequencies and fitness parameters. Setting \( r = \frac{1}{2} \), however, remains the sufficient condition for the maintenance of linkage equilibrium in the multiplicative case, even before the allele frequency equilibrium is reached.

A polymorphic 2-locus equilibrium in the multiplicative fitness case, which represents a pair of one-locus polymorphisms similar to (4) in the Model 1, exists and retains its stability conditions even when the loci do not recombine freely and the initial \( D \neq 0 \). For any \( D_m, D_f \) and \( r \), but letting \( w_{i,3} = 1 \) and \( w_{i,4} = w_{i,1} w_{i,2} \), the Jacobian of the system of recurrence equations (5) is:

\[
\begin{pmatrix}
\frac{w_{m,1}}{2(1 - p_m (1 - w_{m,1}))^2} & 1/2 & 0 & -\left( 1 - w_{m,2} \right)^2 D_f / 2 \left( 1 - u_f (1 - w_{m,2}) \right)^2 \\
\frac{w_{f,1}}{2(1 - p_m (1 - w_{f,1}))^2} & 1/2 & 0 & -\left( 1 - w_{f,2} \right)^2 D_f / 2 \left( 1 - u_f (1 - w_{f,2}) \right)^2 \\
-\left( 1 - w_{m,1} \right)^2 D_m / 2 \left( 1 - p_m (1 - w_{m,1}) \right)^2 & 0 & 1/2 & w_{m,2} / 2 \left( 1 - u_f (1 - w_{m,2}) \right)^2 \\
-\left( 1 - w_{f,1} \right)^2 D_m / 2 \left( 1 - p_m (1 - w_{f,1}) \right)^2 & 0 & 1/2 & w_{f,2} / 2 \left( 1 - u_f (1 - w_{f,2}) \right)^2
\end{pmatrix}
\]

(A3)
This matrix is independent of the recombination rate $r$, and since $D_m, D_f = 0$ at equilibrium, the corresponding elements in the top right and bottom left of the matrix become zero. Thus the remaining elements at the bottom right and top left corners of the matrix independently determine the local stability of the $A/a$ and $B/b$ locus, respectively.

Further substitutions: $w_{m,1} \rightarrow 1 - t$, $w_{f,1} \rightarrow 1 - s$ and $p_m \rightarrow 1 - p_m$ bring the top left corner of (A3) to the form identical to (4) in ANDERSON AND SPENCER (1999), which suggests that the stability conditions derived therein remain exactly the same.
<table>
<thead>
<tr>
<th>Zygote</th>
<th>Gametes / haploids</th>
<th>Frequency before selection</th>
<th>Fitness male</th>
<th>Fitness female</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A)A</td>
<td>A</td>
<td>$p_f p_m$</td>
<td>$1 - \alpha$</td>
<td>$1 - \delta$</td>
</tr>
<tr>
<td></td>
<td>$\frac{1}{2} A$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(A)a</td>
<td>$\frac{1}{2} a$</td>
<td>$p_f (1 - p_m)$</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>(a)A</td>
<td>$\frac{1}{2} A$</td>
<td>$(1 - p_f) p_m$</td>
<td>$1 - \alpha$</td>
<td>$1 - \delta$</td>
</tr>
<tr>
<td>(a)a</td>
<td>A</td>
<td>$(1 - p_f) (1 - p_m)$</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

* Parentheses in the first column indicate maternal genotype (parental selection model) or inactivation of maternally derived allele (imprinting model). Whether selection occurs at the diploid (first column) or subsequent haploid (second column) stage does not change the resulting allele frequencies.
Table 2
Offspring genotypic proportions from different mating types, sorted among four phenotypic groups / combinations of maternal and paternal effects, Model 2

<table>
<thead>
<tr>
<th>Parental genotypes</th>
<th>Offspring genotypes / phenotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>male</td>
</tr>
<tr>
<td>Paternal (( \phi = 1 ))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AB</td>
</tr>
<tr>
<td></td>
<td>Ab</td>
</tr>
<tr>
<td></td>
<td>aB</td>
</tr>
<tr>
<td></td>
<td>ab</td>
</tr>
<tr>
<td>Joint (( \phi = 4 ))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AB</td>
</tr>
<tr>
<td></td>
<td>Ab</td>
</tr>
<tr>
<td></td>
<td>aB</td>
</tr>
<tr>
<td></td>
<td>ab</td>
</tr>
<tr>
<td>Maternal (( \phi = 2 ))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AB</td>
</tr>
<tr>
<td></td>
<td>Ab</td>
</tr>
<tr>
<td></td>
<td>aB</td>
</tr>
<tr>
<td></td>
<td>ab</td>
</tr>
<tr>
<td>None (( \phi = 3 ))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AB</td>
</tr>
<tr>
<td></td>
<td>Ab</td>
</tr>
<tr>
<td></td>
<td>aB</td>
</tr>
<tr>
<td></td>
<td>ab</td>
</tr>
<tr>
<td>ab</td>
<td>(1)</td>
</tr>
</tbody>
</table>
Table 3

Genotype frequencies in parents expressed through allele frequencies, Model 2

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>Ab</th>
<th>aB</th>
<th>Ab</th>
</tr>
</thead>
<tbody>
<tr>
<td>males</td>
<td>( F_m )</td>
<td>( p_m u_m + D_m )</td>
<td>( p_m v_m - D_m )</td>
<td>( q_m u_m - D_m )</td>
</tr>
<tr>
<td>females</td>
<td>( F_f )</td>
<td>( p_f u_f + D_f )</td>
<td>( p_f v_f - D_f )</td>
<td>( q_f u_f - D_f )</td>
</tr>
</tbody>
</table>
Fig. 1
Fig. 2

\[ \alpha = \frac{\delta}{2\delta - 1} \]

\[ \alpha = \frac{-\delta}{2\delta + 1} \]

Ab fixed

aB fixed
Fig. 3
Fig. 4
**Fig. 1.** Geometrical representation of genotype frequencies in a haploid 2-locus system. The population at any time is described by two points in a tetrahedron, one each for males and females (shown exaggeratedly different). The corners of the tetrahedron are fixation equilibria, the edges marked by the gray and by the black lines are the equilibria fixed at $A/a$ and $B/b$ loci, respectively, and polymorphic for the other locus. The space within the tetrahedron shows all possible 2-locus polymorphisms in the population.

**Fig. 2.** Stability of equilibria in the fitness parameter space under the assumption of antagonistic selection between phenotypes, special case (i) of the additive fitness scheme. Fixations for $Ab$ and $aB$ genotypes are stable above $\alpha = \frac{-\delta}{2\delta + 1}$ and below $\alpha = \frac{\delta}{2\delta - 1}$ lines, respectively. The space in between the lines represents stability range of the 2-locus polymorphism. The dashed line $\alpha = -\delta$ divides the stability ranges of the internal (4) and fixation ($p = 0$) equilibria in the single-locus Model 1 (see text).

**Fig. 3.** Stability of equilibria in the fitness parameter space under the assumption of equality of maternal and paternal effects, special case (ii). The solid line is $\alpha = -\delta$, the other two represent $\alpha = \frac{\delta}{2k\delta - 1}$ for $t = 2$ (thick dashed line) and $t = \frac{1}{2}$ (thin dashed line). At the point $(\delta = 0.34, \alpha = -0.42)$ only a 2-locus polymorphism is stable for $t = 2$ but both fixation for $AB$ genotype and the 2-locus polymorphism are stable for $t = \frac{1}{2}$.

**Fig. 4.** Examples of shifts of the model’s equilibria by selection on the individual’s own genotype. The dashed and solid lines are the frequencies $p$ and $u$ of $A$ and $B$ alleles,
respectively, averaged between sexes, at equilibrium. Additive parental selection parameters are: $\alpha = 0.14$, $\beta = -0.1$, $\delta = -0.12$, $\gamma = 0.11$. The viability fitness $G_2$ of the genotypes containing $B$ allele is varied, as the viability $G_1$ of $A$ genotypes is kept constant and shown at the top of each plot; A – change from fixation $AB$ to the $Ab-ab$ edge equilibrium, B – change from $AB-Ab$ to $AB-aB$ edge equilibrium, C – change from $AB-Ab$ edge to $ab$ fixation equilibrium