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What are maternal effects (and what are they not)?

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Maternal effects can play an important role in a diversity of ecological and evolutionary processes such as population dynamics, phenotypic plasticity, niche construction, life-history evolution and the evolutionary response to selection. However, although maternal effects were defined by quantitative geneticists well over half a century ago, there remains some confusion over exactly what phenomena should be characterized as maternal effects and, more importantly, why it matters and how they are defined. We suggest a definition of maternal effects as the *causal* influence of the maternal genotype or phenotype on the offspring phenotype. This definition differs from some definitions in that it treats maternal effects as a phenomenon, not as a statistical construct. The causal link to maternal genotype or phenotype is the critical component of this definition providing the link between maternal effects and evolutionary and ecological processes. We show why phenomena such as maternal cytoplasmic inheritance and genomic imprinting are distinct genetically from and have different evolutionary consequences than true maternal effects. We also argue that one should consider cases where the maternal effect is conditional on offspring genotype as a class of maternal effects.

Keywords: maternal inheritance; genomic imprinting; maternal–zygotic epistasis; cross-fostering; indirect effects

1. INTRODUCTION

The importance of maternal effects has long been recognized by quantitative geneticists (e.g. Dickerson 1947), although they have largely regarded them as non-genetic environmental sources of resemblance of relatives (e.g. Falconer & Mackay 1996, p. 156; Futuyma 1998, p. 233) and a nuisance that contaminates estimates of heritability (cf. Wade 1998). Quantitative geneticists have historically defined maternal effects as the influence of the maternally provided environment on the phenotype of her offspring (Dickerson 1947; Willham 1963, 1972; Legates 1972; Cheverud 1984). This view of maternal effects has led to the development of various quantitative genetic models of phenotypic evolution that explicitly include maternal effects (e.g. Dickerson 1947; Willham 1972; Cheverud 1984; Kirkpatrick & Lande 1989). The growth of interest in maternal effects in quantitative genetics has led to a broader interest in maternal effects in a variety of other areas, such as population biology, phenotypic plasticity (Donohue & Schmitt 1998; Mousseau & Fox 1998*b*), life-history evolution (e.g. Kaplan 1991; Mousseau & Dingle 1991) and various other aspects of plant and animal ecology (see Bernardo 1996; Mousseau & Fox 1998*a*) such as population dynamics (e.g. Ginzburg & Taneyhill 1994; Rossiter 1994; Ginzburg 1998) and niche construction (Odling-Smee *et al.* 2003; Donohue *et al.* 2005).

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One contribution of 12 to a Theme Issue 'Evolution of parental effects: conceptual issues and empirical patterns'.

Although maternal effects were defined by quantitative geneticists well over half a century ago, there remains some confusion over exactly what phenomena should be characterized as maternal effects and, more importantly, why it matters to evolutionary biology how they are defined. This confusion stems in a large part from the erroneous interpretation of maternal effects as being synonymous with the broader phenomenon of maternal inheritance (e.g. Kirkpatrick & Lande 1989). One particularly conspicuous error, frequent in the medical literature of human genetics, is the interpretation of the phenotypic effects of mitochondria as 'maternal effects' (e.g. Korpelainen 1999; Yang *et al.* 2007). Similarly, the simple definition of maternal effects is often extended to incorporate a diversity of other related phenomena (e.g. kin effects, genomic imprinting, uniparental extra-chromosomal inheritance). Therefore, we endeavour to put forth a single and general definition of maternal effects that does not confound maternal effects with any other related phenomena. We do so because, despite the fact that they may be conceptually related, these various other phenomena have genetic and evolutionary consequences distinct from maternal effects. Throughout, we discuss maternal effects for convenience while reminding the reader that the discussion is equally applicable to paternal effects.

We define maternal effects as the *causal* influence of the maternal genotype or phenotype on the offspring phenotype. Although we are not aware of any previous publications that have invoked this exact same definition, we nevertheless emphasize that our definition agrees conceptually (at least in part) with

definitions used by a variety of authors (e.g. Lacy 1998; Roff 1998). This definition leads to a simple statement of the evolutionary importance of maternal effects—evolutionary changes in the distribution of maternal traits (i.e. genotypes or phenotypes) will cause evolutionary changes in some offspring traits due to the causal influence of those maternal traits on those offspring traits. This precludes, of course, the evolutionary change simply resulting from changes in the distribution of directly inherited genotypes from those parents.

Many definitions in the literature are statistical in nature and are focused on the detection or partitioning of maternal effects as one among a variety of other causal components of phenotypic variation among a set of individuals, generally offspring. Our definition begins with a phenomenological view of a maternal effect as a causal mechanism, independent of how one might actually detect or analyse such effects or partition them into maternal environmental and maternal genetic components. Therefore, we do not include caveats or extensions such as a requirement that these effects be independent of offspring phenotype or genotype, or are defined while holding offspring genotype constant. This is because the definition explicitly includes the fact that the influence must be causal, and, therefore, requirements that they are 'independent of' or are measured 'while holding constant' offspring genotype are not necessary and, in many cases, may simply not be the case. The mechanism for this maternal influence is generally through the maternally provided 'environment', whether in the form of maternal messenger RNAs that are pre-loaded into the unfertilized egg or ovule, or in the form of post-zygotic influences via maternal traits such as nutritional provision, behavioural choice of nesting sites, materials and construction in animals, and seed architecture and dispersal traits in plants (Howe & Smallwood 1982; Primack 1987; Chambers & MacMahon 1994). The critical aspect is the causal link between maternal features (traits or loci) and offspring phenotypes. For example, maternal oviposition site choice in many animals (e.g. insects; Resetarits 1996; Mousseau & Fox 1998*c*) can have important influences on the offspring phenotype, but the actual effects are often attributable to some ecological aspect of the environment where the eggs are laid. Similarly, in plants, maternally determined seed architecture often determines where and how long after dispersal a seed germinates (Chambers & MacMahon 1994; Galloway 2005), even in those cases where seeds are animal distributed. Some plant species have maternally determined alternative seed morphs (Donohue 1998) as well as alternative life histories (Boyd *et al.* 2007). In such cases, the influence on the offspring phenotype could be attributed to the maternal oviposition site choice behaviour or seed architecture, where the ultimate effect of mothers on their offspring is mediated via the ecological environment. Like mate choice in sexual selection, however, discriminating choice from chance in oviposition may well be difficult experimentally.

It is important to remember that all maternal effects are ultimately mediated through the maternal phenotype (even when that phenotype is a simple RNA molecule or protein) and thus, like essentially all traits, are likely to be influenced by both genetic and environmental sources of variation (including genotype-by-environment interactions). This raises another important difference between animals and plants, or more narrowly, between species with separate sexes (many animals but few plants) and dioecious or hermaphroditic species (many plants and some animals). Every individual in the latter is a mother and may perpetrate maternal effects on the offspring, in contrast to species with separate sexes, wherein only half of the individuals are mothers expressing maternal effects.

There may also be cases where it is difficult to separate an influence on the offspring phenotype into an independent maternal effect and direct effect of the offspring's own genotype or environment. For example, the placenta is clearly an important potential source of maternal effects in mammals (e.g. Cowley *et al.* 1989; Cowley 1991) and presumably in other species with placentas such as Poeciliid fishes (Reznick *et al.* 2002), but it is not exclusively a maternal trait given the joint influence of the offspring and maternal genomes. Indeed, whenever there are maternal–zygotic interactions, it will not be possible to statistically attribute the interaction variance to either a maternal or zygotic cause (Wolf 2000; Priest & Wade in press). Although such a separation may be statistically problematic, there is still a causal influence of a maternal feature on offspring phenotype, which we call a maternal effect.

Under our definition, maternal effects may result directly as a consequence of maternal traits, such as nursing (e.g. Gouldsborough *et al.* 1998), provisioning or licking/grooming of offspring by mothers (e.g. Cameron *et al.* 2008*a*,*b*), whether seeds are developed cleistogamously or chasmogamously and dispersed passively or explosively (e.g. Stamp 1989; Berg 2000) or may result indirectly from maternal traits such as when mothers lay eggs or disperse seeds in particular environments and these environments, in turn, have effects on offspring traits (e.g. effects of oviposition site choice on offspring sex in species with environmental sex determination; Roosenburg & Niewiarowski 1998; maternal provisioning and its effects on the quality of larval food; Fox & Mousseau 1996; or the opportunity for kin selection among seedlings; Dudley & File 2007). These effects can be further mediated through offspring traits, such as the plastic response of developing dung beetles to environmental quality resulting in both horned and hornless males (Hunt & Simmons 2000) or in offspring response to maternal behaviour, such as begging in birds (Henderson 1975) or burying beetles (Lock *et al.* 2007).

Our goal is to clearly distinguish the phenomena that are often erroneously clustered with maternal effects from true maternal effects in terms of their genetic and evolutionary consequences. While we focus on just a few main phenomena, our goal is to build a conceptual framework that can be used to analyse other phenomena not discussed herein. We refer the reader to other reviews of maternal effects (Wade 1998;

Cheverud & Wolf 2009; Wade *et al.* in press) for additional discussion of the definition, genetics and evolutionary consequences of maternal effects. Throughout, we use the tools of quantitative genetics implemented through one- and two-locus models to illustrate our points. The results based on these models apply, for the most part, equally well to other more complex genetic systems.

2. WHAT MATERNAL EFFECTS ARE *NOT*

(a) *Maternal cytoplasmic inheritance is not a maternal effect*

Perhaps the most common phenomenon confounded with maternal effects is the broader phenomenon of maternal inheritance, which is problematic when cytoplasmic inheritance (e.g. inheritance of organelles) is not distinguished from other non-genetic forms of maternal influence (e.g. Mather & Jinks 1971; Kirkpatrick & Lande 1989; Thiede 1998; Korpelainen 1999; Reinhold 2002). Maternal inheritance most often refers to the case where individuals inherit some factor from only their mothers, but we distinguish maternal cytoplasmic inheritance to specifically refer to organelle inheritance via the egg. In most cases of uniparental inheritance, the offspring are genetically identical (other than new variation caused by mutation) to their mothers with respect to their cytoplasmic genotype. An example of a maternally inherited locus is given in table 1, which illustrates the simple cases where there is a single locus with two alternative alleles that directly affect some trait (i.e. the cytoplasmic genotype of an individual influences that individual's phenotype). Such a pattern of maternal inheritance increases the resemblance between offspring and mother compared with that between offspring and father, and therefore may appear statistically along with other true maternal effects in quantitative genetic or other analyses. This is due to the increased relatedness (i.e. generally a relatedness of 1) between the maternal and offspring cytoplasmic genotypes (seen by the perfect correlation between maternal and offspring genotypes in table 1). Conceptually, it is easy to see why such a pattern is distinct from a true maternal effect; the offspring cytoplasmic genotype causes all variation in the offspring phenotype. Owing to the perfect correlation between maternal and offspring cytoplasmic genotypes, this variation among offspring of different families cannot be partitioned into separate causal influences within families. However, despite this absolute co-linearity, it is clear that after the offspring cytoplasmic genotype accounts for the phenotypic variation, there would be no variation left over to account for in terms of variations among the maternal cytoplasmic genotypes. That is, the maternal genotype and phenotype have no *causal* influence on the offspring phenotype, and therefore such maternal inheritance is clearly not a maternal effect.

The case of strict maternal inheritance is probably the most problematic (and insidious) phenomenon confounded with maternal effects because it requires cross-fostering to break apart the inherent correlation between maternal and offspring genotype (Roff 1998).

Table 1. An example of a cytoplasmic maternally inherited locus. (The locus has two alleles, M_1 and M_2, with frequencies p_1 and p_2 that have genotypic values $+m$ and $-m$, respectively. The cells show the expected phenotypes and frequencies (in parentheses) of offspring with each of the two cytoplasmic genotypes. Cells with a frequency of zero are maternal–offspring cytoplasmic genotype combinations that cannot exist under strict maternal inheritance. The column labelled $\bar{z}_{\text{maternal}}$ gives the mean phenotypes of offspring produced by the maternal genotypes while $\bar{z}_{\text{offspring}}$ gives the mean phenotypes of offspring with the two cytoplasmic genotypes.)

		offspring genotype		
		M_1	M_2	$\bar{z}_{\text{maternal}}$
maternal genotype	M_1	$+m$ (p_1)	(0)	$+m$
	M_2	(0)	$-m$ (p_2)	$-m$
$\bar{z}_{\text{offspring}}$		$+m$	$-m$	

Such cross fostering across cytoplasmic genotypes is either impractical or impossible in most systems. However, although difficult (or perhaps impossible) to separate real maternal effects from maternal inheritance in many (or most) systems, the distinction is critical if one wishes to understand the causal origin of phenotypic variation or to understand the evolutionary dynamics of traits. This distinction is critical, for example, in quantitative genetic models of maternal effects (e.g. Kirkpatrick & Lande 1989) and the theory will fail to predict the evolutionary response to selection if supposed maternal effect variation is actually caused by cytoplasmic inheritance. For instance, the evolutionary time-lags that attend the response to selection on maternal effects do not occur when the variation targeted by selection is caused by the direct effects of maternally inherited cytoplasmic genes because there is no influence of the previous generation's phenotype on that of the current generation.

(b) *Genomic imprinting is not a maternal effect*

Genomic imprinting refers to the phenomenon where individuals express only the maternally or the paternally inherited copy of an allele. More generally, it refers to parent-of-origin dependent gene expression or effects (see Bartolomei & Tilghman 1997; Reik & Walter 2001). Various researchers have suggested that genomic imprinting should be considered a form of parental effect in the sense that it is a parental effect on gene expression (e.g. Lacy 1998). In order to categorize imprinting in a way consistent with our definition of maternal effects, we need to distinguish between the genes in the maternal genome that cause the imprinting and the genes in the offspring genome that become imprinted. The former are maternal effect genes and have evolutionary properties similar to those of other genes with maternal effects on the offspring phenotype. The latter are genes in the zygotic genome with direct effects on the offspring phenotype. Thus, we believe that it is a mistake to lump the entire phenomenon of imprinting with maternal (or more generally parental) effects. This is because the direct effect of the offspring genotype accounts for all of the genetic variance in the expression of the offspring trait, and therefore there is

Table 2. An example of an imprinted locus showing maternal expression. (The locus has two alleles, A_1 and A_2, with frequencies p_1 and p_2. The expected phenotypes and frequencies (in parentheses) of offspring with each of the four ordered genotypes (given as paternally inherited allele followed by maternally inherited allele) are shown for the eight maternal–offspring genotype combinations. Cells with a frequency of zero are maternal–offspring genotype combinations that cannot exist (e.g. an A_1A_2 individual cannot get the A_2 allele from their mother). Offspring express the maternally inherited allele, those expressing the A_1 allele have phenotype $+i$ while those expressing the A_2 allele have phenotype $-i$. The column labelled $\bar{z}_{\text{maternal}}$ gives the mean phenotypes of the offspring produced by the three maternal genotypes while $\bar{z}_{\text{offspring}}$ gives the mean phenotypes of the offspring with each of the four ordered genotypes.)

		offspring genotype				
		A_1A_1	A_2A_1	A_1A_2	A_2A_2	$\bar{z}_{\text{maternal}}$
maternal genotype	A_1A_1	$+i\,(p_1^3)$	$+i\,(p_1^2p_2)$	(0)	(0)	$+i$
	A_1A_2	$+i\,(p_1^2p_2)$	$+i\,(p_1p_2^2)$	$-i\,(p_1^2p_2)$	$-i\,(p_1p_2^2)$	0
	A_2A_2	(0)	(0)	$-i\,(p_1p_2^2)$	$-i\,(p_2^3)$	$-i$
$\bar{z}_{\text{offspring}}$		$+i$	$+i$	$-i$	$-i$	

no variation explained by the maternal genotype (see Spencer 2002; Santure & Spencer 2006; Hager *et al.* 2008). In specific cases, where imprinting is controlled by a maternal trait or locus, there is a causal link to the maternal genotype and the offspring genotype does not account for all the variance.

To understand why the simple parental expression of alleles (i.e. maternal or paternal expression that refers to the parent-of-origin of the alleles expressed by offspring) is not a parental effect, we will use the example of maternal expression of a locus (i.e. the paternally inherited allele is silenced). We assume, for simplicity, that the locus has two alleles. We designate the alleles at the locus A_1 and A_2 that have frequencies p_1 and p_2, respectively (table 2). Since we wish to illustrate imprinting effects, we distinguish the two heterozygotes that differ with regard to parent of origin of alleles, with the paternal allele listed first. For example, the A_2A_1 genotype received the A_1 allele from the mother and the A_2 allele from the father. Assuming a large randomly mating population with no selection, the frequencies of the four ordered genotypes are given by the expansion of the quadratic $(p_1+p_2)^2$. To model maternal expression, we assume that individuals that get the A_1 allele from their mothers have the phenotype $+i$ and those that get the A_2 allele from their mothers have the phenotype $-i$ (Spencer 2002 for a discussion of parameterizing imprinting effects).

From the average phenotypes of the offspring of the three maternal genotypes (designated $\bar{z}_{\text{maternal}}$) it may appear that there is a maternal effect since the mean phenotypes of offspring produced by the different types of mothers match the pattern of genetic effects (i.e. A_1A_1 mothers have $+i$ offspring while A_2A_2 mothers have $-i$ offspring). However, if we look at the average phenotypes of the four ordered genotypes of offspring (designated $\bar{z}_{\text{offspring}}$) we see that, as expected, the pattern matches the assumed pattern of genetic effect, where individuals receiving the A_1 allele from their mothers have the $+i$ phenotype and those receiving the A_2 allele have the $-i$ phenotype. The maternal genotype explains variation in the average offspring phenotype in this case, simply because of the correlation between parent and offspring genotypes caused by ordinary autosomal inheritance (i.e. it is caused by the fact that there are missing maternal–offspring genotype combinations, that are cells with a frequency of zero in table 2). The lack of a causal relationship can be seen when we regress offspring phenotype on the maternally inherited allele in offspring ($+1$ for A_1 and -1 for A_2) and find a coefficient of i, with the offspring genotype accounting for a variance of $4\,p_1p_2i^2$, which is the total phenotypic variance. By contrast, if we regress offspring phenotype on maternal genotype (using $A_1A_1=1$, $A_1A_2=0$ and $A_2A_2=-1$), we also find a coefficient of i but the maternal genotype only accounts for $2p_1p_2i^2$ of the variance. This means that, if we first regress offspring phenotype on maternal genotype and then use the residuals to regress on offspring genotype, we find that the offspring genotype still accounts for variation, with a coefficient of $i/2$ accounting for a variance of $2p_1p_2i^2$ (so the maternal genotype only removes half the relationship owing to the correlation between maternal and offspring genotypes of one-half, the value for any Mendelian diploid gene). By contrast, if we first regress offspring phenotype on offspring genotype and then regress the residuals on maternal genotype, we find that the regression coefficient is zero because there is no residual variation, i.e. offspring genotype accounts for all variation in offspring phenotype, as long as we consider the parent of origin of alleles.

The fact that imprinting is not a maternal effect is also clear, if we look at the offspring of the A_1A_2 mothers in table 2. These offspring all have genetically identical mothers but have different phenotypes depending on the parent of origin of their alleles. Since there is no variation in the genotypes of their mothers, the pattern of gene expression cannot be caused by a maternal effect (Hager *et al.* 2008). Indeed, this pattern of parent-of-origin dependent effects in offspring from genetically identical mothers has been suggested as the key genetic signature that can be used to differentiate true genomic imprinting effects from the confounded pattern produced by a maternal effect (Hager *et al.* 2008).

If, however, there is a locus in mothers that controls the imprinting state of another locus in her offspring (e.g. Grossniklaus *et al.* 2001; Duselis *et al.* 2005), perhaps through some maternal behaviour (Weaver *et al.* 2004), then there can be a maternal effect on the pattern of gene expression and imprinting itself would

Table 3. An example of a system where imprinting of a locus in offspring is controlled by the maternal genotype. (The locus expressed in offspring has two alleles, A_1 and A_2, with frequencies p_1 and p_2 while the maternal genotype is defined by a second locus that has two alleles, B_1 and B_2, with frequencies x_1 and x_2. The cells show the expected phenotypes and frequencies (in parentheses) of offspring for each of the 12 maternal–offspring genotype combinations (where offspring genotypes are given as paternally inherited allele followed by maternally inherited allele). The locus shows imprinting with maternal expression in offspring of the B_1B_1 mothers, but biallelic expression with an additive effect in the offspring of other mothers. The A_1 allele has a $+a$ effect on the offspring phenotype while the A_2 allele has a $-a$ effect. The column labelled $\bar{z}_{\text{maternal}}$ gives the mean phenotypes of offspring produced by the three maternal genotypes at the B locus while $\bar{z}_{\text{offspring}}$ gives the mean phenotypes of offspring with each of the four ordered genotypes at the A locus.)

		offspring genotype				
		A_1A_1	A_2A_1	A_1A_2	A_2A_2	$\bar{z}_{\text{maternal}}$
maternal genotype	B_1B_1	$+a\ (p_1^2x_1^2)$	$+a\ (p_1p_2x_1^2)$	$-a\ (p_1p_2x_1^2)$	$-a\ (p_2^2x_1^2)$	$+a\ (p_1-p_2)$
	B_1B_2	$+a\ (p_1^2 2x_1x_2)$	$0\ (p_1p_2 2x_1x_2)$	$0\ (p_1p_2 2x_1x_2)$	$-a\ (p_2^2 2x_1x_2)$	$+a\ (p_1-p_2)$
	B_2B_2	$+a\ (p_1^2x_2^2)$	$0\ (p_1p_2x_2^2)$	$0\ (p_1p_2x_2^2)$	$-a\ (p_2^2x_2^2)$	$+a\ (p_1-p_2)$
$\bar{z}_{\text{offspring}}$		$+a$	$+ax_1^2$	$-ax_1^2$	$-a$	

be caused by a maternal effect. Such a scenario is illustrated in table 3, where a second locus expressed in females (locus B) with alleles B_1 and B_2 (and frequencies x_1, x_2) determines if the A locus is imprinted in a female's offspring. For simplicity, we assume that the A and B loci are unlinked (though the implications of this scenario are not affected by linkage disequilibrium). We assume that the A locus has an additive effect (denoted a) on a trait and that monoallelic expression caused by imprinting produces the same phenotype as biallelic expression in a homozygote. We assume that only the offspring of B_1B_1 mothers show imprinting with maternal expression at the A locus, so that the offspring of other mothers show an additive effect.

Unlike the case of regular maternal expression shown in table 2, the maternal genotype accounts for no variance in the phenotypes of the offspring, despite the fact that the maternal genotype determines the imprinting state of the A locus in offspring. The offspring genotype accounts for $2a^2p_1p_2(1+x_1^4)$ of the total variance of $2a^2p_1p_2(1+x_1^2)$, meaning that a variance of $2a^2p_1p_2(x_1^2-x_1^4)$ would appear as an interaction variance between maternal and offspring genotypes, even though we are assuming that the maternal genotype is causing a change in the gene expression independent of the offspring genotype.

This latter scenario highlights a complicating phenomenon in the analysis of maternal effects, namely, there can be variation in offspring traits that depends on the combination of maternal and offspring genotypes. Although, this appears as a maternal genotype by offspring genotype interaction variance (Wade 1998; Wolf 2000), it is also as a type of maternal effect if the maternal genotype or phenotype is causing a change in the pattern of gene expression or genetic effects in offspring (see below), as in the scenario illustrated in table 3. One way to resolve this issue is to view the mean offspring phenotype of the different maternal genotypes in terms of the pattern of genetic effects or gene expression. In the case of genomic imprinting illustrated in table 3, we can characterize the imprinting effect as the imprinting genotypic value. The imprinting genotypic value is half the difference between the mean phenotypes of the ordered heterozygotes (Wolf *et al.* 2008) and is analogous to the additive genotypic value, which is half the difference between homozygote phenotypes. The imprinting genotypic value of B_1B_1 mothers is $+a$ if it is measured as the difference between individuals receiving the A_1 allele from their mothers and those that receive the A_2 allele. For the other two maternal genotypes, the imprinting genotypic value is zero since there is no difference between the two ordered heterozygotes. So we see that, although the maternal genotype explains no variation in offspring phenotype, it explains all the variation in the pattern of genetic effect, and therefore we could call this a maternal effect on the imprinting pattern (i.e. the maternal genotype determines the imprinting genotypic value). Despite the fact that this appears as an interaction effect between maternal and offspring genotypes, we would classify this as a maternal effect because we know that it is the maternal genotype that *causes* the change in expression pattern.

It is important to keep in mind that the distinction between genomic imprinting and true maternal effects is not merely a semantic issue. Since the maternal phenotype or genotype plays no causal role in the expression of the offspring phenotype in the simple case of maternal expression (as in table 2), maternal effects models will not predict the evolutionary dynamics of traits affected by imprinting. However, imprinting contributes to the resemblance of relatives (including both parents and offspring and siblings) and can have important effects on evolutionary dynamics (see Spencer 2000, 2002), and so understanding the contribution of genomic imprinting as opposed to maternal effects is important if one wishes to understand trait evolution (Santure & Spencer 2006). While genomic imprinting is confounded with maternal effects since it can make the maternal–offspring resemblance greater than the paternal–offspring resemblance (Spencer 2002), there are quantitative genetic (see Spencer 2002; Santure & Spencer 2006) and population genetic (see Hager *et al.* 2008) approaches that one can use to separate these two types of effects (though Spencer 2002 points out that some of those approaches may lack adequate power). However, in many standard approaches to detecting maternal effects (such as testing for a difference in the

Table 4. An example of an interaction between the maternal and zygotic genotypes. (The locus expressed in offspring has two alleles, A_1 and A_2, with frequencies p_1 and p_2 while the maternal genotype is defined by a second locus that has two alleles, B_1 and B_2, with frequencies x_1 and x_2. The cells show the expected offspring (zygotic) phenotypes and the frequencies (in parentheses) of the nine maternal–offspring genotype combinations. The locus shows an additive-by-additive interaction effect, where the additive maternal effect depends on the offspring genotype and vice versa. The A_1 allele has a $+a$ effect on the offspring phenotype while the A_2 allele has a $-a$ effect. The column labelled $\bar{z}_{\text{maternal}}$ gives the mean phenotypes of offspring produced by the three maternal genotypes at the B locus while $\bar{z}_{\text{offspring}}$ gives the mean phenotypes of the three offspring genotypes at the A locus.)

		offspring genotype			
		A_1A_1	A_2A_1	A_2A_2	$\bar{z}_{\text{maternal}}$
maternal genotype	B_1B_1	$+a$ $(p_1^2x_1^2)$	0 $(2p_1p_2x_1^2)$	$-a$ $(p_2^2x_1^2)$	$+a(p_1 - p_2)$
	B_1B_2	0 $(p_1^2 2x_1x_2)$	0 $(2p_1p_2 2x_1x_2)$	0 $(p_2^2 2x_1x_2)$	0
	B_2B_2	$-a$ $(p_1^2x_2^2)$	0 $(2p_1p_2x_2^2)$	$+a$ $(p_2^2x_2^2)$	$-a(p_1 - p_2)$
$\bar{z}_{\text{offspring}}$		$+a(x_1-x_2)$	0	$-a(x_1-x_2)$	

maternal– versus paternal–offspring regressions) the two effects will remain confounded, and therefore it is important to recognize that patterns interpreted as maternal effects can result from genomic imprinting (and vice versa, e.g. Hager *et al.* 2008).

In the case of maternal control of the imprinting status of a locus in offspring (i.e. where variation in the pattern of gene expression is determined by the maternal genotype), viewing the phenomenon as a maternal effect makes sense from an evolutionary point of view. That is, understanding the evolution of the maternal traits or allele frequencies at loci that determine imprinting status allows one to understand evolutionary changes in expression patterns, i.e. imprinting process evolves as a maternal effect. Thus, when one discusses imprinting as a maternal effect it is critical to ask whether they are referring to a maternal effect on imprinting, or the simple case of an imprinted gene showing maternal expression.

(c) *Maternal effects need not be independent of offspring genotype*

As noted above, many authors invoke a statistical definition of maternal effects in the context of partitioning variation among offspring phenotypes that requires maternal effects to be independent of offspring genotype effects (e.g. Mousseau & Fox 1998*c*; Price 1998; Altmann & Alberts 2005; Dloniak *et al.* 2006; Nye *et al.* 2007), regardless of the underlying mechanism. This may be the consequence of a statistical description that defines maternal effects as the influence of the maternal phenotype on offspring phenotype holding *offspring genotype constant*, as seen in regression analyses of maternal effects (e.g. Kirkpatrick & Lande 1989). However, because maternal effects are a description of a causal phenomenon they need not satisfy such a statistical constraint, even if invoking such a definition is useful in empirical analyses. There are a number of reasons to believe that maternal effects may often depend on offspring genotype (Wolf 2000) and that the two will show an interaction effect as in table 3. A simple example is where there is an 'additive-by-additive' interaction between the maternal and offspring genotype (see Wade 1998; Wolf 2000). This pattern is shown in table 4, where the A_1 allele has a positive additive effect of $+a$ in the offspring of B_1B_1 mothers, no effect in the offspring of B_1B_2 mothers and an effect of $-a$ in the offspring of B_2B_2 mothers. Without knowledge of the causal origin of the interaction effect, this situation can also be viewed as a change in the maternal effect depending on offspring genotype, where the B_1 allele has a positive additive maternal effect of $+a$ on offspring of the A_1A_1 genotype, no effect on offspring of the A_1A_2 genotype and a maternal effect of $-a$ on offspring of the A_2A_2 genotype.

The interaction between maternal and offspring genotypes on the offspring phenotype makes the additive direct effect (i.e. the additive genotypic value that is half the difference between the phenotypes of the homozygotes; see Falconer & Mackay 1996) of the A locus (which has the value $a(x_1-x_2)$) and the additive maternal effect of the B locus (which has the value $a(p_1-p_2)$) entirely dependent on the allele frequency at the other locus. Consequently, the maternal effect variance (i.e. the variance among the mean offspring of the different maternal genotypes), which is equal to $2a^2x_1x_2(p_1-p_2)^2$, and the variance among mean offspring genotypic values, which is equal to $2a^2p_1p_2(x_1-x_2)^2$, are both entirely attributable to the physiological interaction (cf. Cheverud & Routman 1995) between maternal and offspring genotypes. That is, the effect of one locus depends upon allele frequencies at the other as in classical epistasis (Wade 2001, 2002). However, this also means that both the A and the B locus will appear to have a main (independent) effect on the offspring phenotype for almost all allele frequencies (as long as the other locus is not fixed or exactly at a frequency of 0.5). As a result, the B locus will almost always appear to have a maternal effect and the A locus will appear to have an independent direct effect.

How we classify the effects in a system similar to that illustrated in table 4 depends on the functional origin of the effects. That is, the marginal effects and variances are statistical ways to view the variation produced by the maternal and direct effects of the A and B loci, but whether we define the loci as having true direct or maternal effects depends on where the effects actually arise from. If the influence of the B locus on the phenotype of the offspring is caused by the maternal

genotype or phenotype, then we would classify the B locus as having a maternal effect, even if the exact effect depends on the offspring's genotype. In this case, we would say that the B locus has a maternal effect, but the effect depends on exactly what sorts of offspring mothers are rearing (or otherwise interacting with or affecting). If mothers are mostly raising A_1A_1 offspring (i.e. the A_1 allele is common, and so $p_1 > p_2$), then the B_1 allele at the B locus has a mainly positive maternal effect, while the opposite is true when mothers are mostly raising A_2A_2 offspring.

We can also view the scenario in table 4, as described above for the imprinting effect, as a case where the B locus has a maternal effect on gene expression or the genetic effect of the A locus in offspring. In offspring of the B_1B_1 mothers, the A_1 allele has a positive additive effect of $+a$ while in offspring of B_2B_2 mothers, the A_1 allele has a negative additive effect of $-a$. Therefore, there is a maternal effect on the additive effect of the A locus. Similar to the case of genomic imprinting controlled by a maternal effect, we can understand the evolution of the effects of alleles at the A locus as being driven by evolution of the maternal effect of the B locus. Owing to the symmetry in the example in table 4, one can also view this as a case where the expression of the A locus in offspring determines the maternal effect of the B locus such that evolution of the maternal effect of the B locus is driven by evolutionary changes at the A locus. Such a case of an epistatic interaction between a maternal effect and a direct effect locus can play a role in evolutionary processes where epistasis has been shown to be important, such as the evolution of genetic effects and the evolution of population differentiation and coadaptation.

3. CONCLUSIONS

Our goal has been to provide a framework that can be used to critically assess whether phenomena are or are not maternal effects. Therefore, we have neither presented a comprehensive analysis of all possible phenomena (if that were even possible) nor a comprehensive review of all things labelled 'maternal effects'. We emphasize that the evolutionary and ecological consequences of maternal effects are distinct from those of the various other phenomena that we would not classify as maternal effects. We argue that an overly broad definition may encompass so many functionally distinct phenomena that it is not useful and, in fact, can obscure the unique evolutionary importance of maternal effects (e.g. Cruickshank & Wade 2008). For example, models of trait evolution that incorporate maternal effects (e.g. Kirkpatrick & Lande 1989) will fail to predict or explain the evolutionary dynamics of traits that are influenced by cytoplasmic effects or genomic imprinting rather than true maternal effects.

In addition to the specific phenomena we analyse herein, there are many other phenomena that have been suggested to be maternal effects, but clearly fail to meet our criteria, such as mate choice by females, where there is a supposed maternal effect on the genes an individual inherits from their father, or where, by choosing mates, females determine the quality of non-genetic contributions by males (Mousseau & Fox 1998*c*). There is also a wide range of phenomena where there may appear to be an effect of parents on their offspring, but the effect actually originates from the interaction between sibs, and therefore, the parents do not play a direct causal role in that variation. When examining these and the countless arrays of other phenomena conceptually related to maternal effects, we suggest that the reader should ask whether they all share features that link their evolutionary importance to those phenomena that have been classically treated as maternal effects. When the answer is 'no', then clearly nothing is gained by expanding the definition to incorporate more and more phenomena, and we may lose our ability to discuss maternal effects as a single phenomenon that has a unified set of evolutionary and ecological implications.

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