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# When is incomplete epigenetic resetting in germ cells favoured by natural selection?

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Resetting of epigenetic marks, such as DNA methylation, in germ cells or early embryos is not always complete. Epigenetic states may therefore persist, decay or accumulate across generations. In spite of mounting empirical evidence for incomplete resetting, it is currently poorly understood whether it simply reflects stochastic noise or plays an adaptive role in phenotype determination. Here, we use a simple model to show that incomplete resetting can be adaptive in heterogeneous environments. Transmission of acquired epigenetic states prevents mismatched phenotypes when the environment changes infrequently relative to generation time and when maternal and environmental cues are unreliable. We discuss how these results may help to interpret the emerging data on transgenerational epigenetic inheritance in plants and animals.

## 1. Introduction

Epigenetic mechanisms produce persistent phenotypic effects. At the cellular level, epigenetics typically refer to molecular mechanisms that are physically associated with DNA and that contribute to gene expression, including histones, DNA methylation and small RNAs. Cells acquire different epigenetic states as part of normal development. To prevent these epigenetic modifications from being passed on to subsequent generations, the life cycle of animals and plants usually involves at least one instance of epigenetic resetting [1–4]. For example, the zygotic DNA in mammals first undergoes extensive de-methylation followed by re-methylation in the early embryo and in the primordial germ cells [3]. In plants, reprogramming may be restricted to the male germline and companion cells, with no global resetting of methylation in seed germ cells [1,2,4,5]. Recent data from both animals and plants indicate that epigenetic resetting is not always complete and hence that acquired epigenetic states may be transmitted from parents to offspring ('germ-line epigenetic inheritance' or 'incomplete epigenetic resetting' or 'incomplete epigenetic reprogramming'; e.g. [6–14] reviewed in [4,5,15–19]).

Is incomplete epigenetic resetting an occasional phenomenon with neutral or negative effects on fitness, or can incomplete resetting be an adaptation [17,20–26]? The consequence of incomplete epigenetic resetting in germ cells is that environmental conditions encountered in one generation can have effects on the development of the next generation or even many generations later. It is generally accepted that effects which span a single generation (parental effects) may increase fitness by adjusting offspring phenotype to local conditions [27–31]. More stable forms of epigenetic inheritance have been suggested to serve a similar function (e.g. [18,21,32,33]).

A number of recent models have explored the evolutionary dynamics of epigenetic inheritance (e.g. [34–36], reviewed in [26]). Most models study how the extent of incomplete epigenetic resetting influences the spread and maintenance of genetic or epigenetic variation. For example, Geoghegan & Spencer [36,37] modelled a two-state environment with epigenetic resetting taking place in the gametes before formation of zygotes, followed by random dispersal and selection.

This model showed that the frequency of environments and the rate of resetting in the gametes jointly determined the likelihood that an epigenetic variant ('epiallele') would invade a resident population. When one environment was rare, resetting according to the environment of the gamete (i.e. the parental environment) produced a phenotype that showed a high likelihood of being mismatched in the next generation, which reduced the likelihood of invasion by the epigenetic variant.

An alternative approach is to let the extent of incomplete resetting evolve as a component of heredity. This is the approach we take in this paper (see also [24,38–40]). Specifically, we develop a simple model of an asexual organism with a single period of epigenetic resetting during germ cell formation. We consider a phenotype that is under selection depending on its match to the environment, and whose expression is determined by the value of an epigenetic state. The environment is both the cause of epigenetic modification and the cause of selection. Using an analytical model and individual-based simulations, we investigate the evolution of incomplete resetting in relation to the rate of environmental change, the specificity of environmental induction of epigenotype and phenotype, and the strength of selection.

## 2. Analytical model

We begin by describing a simple analytical model of a continuous phenotype evolving in a temporally heterogeneous environment, using a similar approach to that of Rivoire & Leibler [38].

### (a) Phenotypes, inheritance and selection

We work with asexual haploids characterized by an epigenetic mark with size $y_t$ in year $t$. The epigenetic state or mark could be, for example, methylation of a DNA sequence (e.g. a promoter) that can vary from completely unmethylated to fully methylated. The epigenetic value translates directly into the phenotype, which is also $y_t$. The environment in year $t$ has state $x_t$, and selection favours a close match between phenotype and state according to a Gaussian fitness function:

$$w(y_t) = w_0 \exp\left[-\frac{1}{2}\frac{(y_t - x_t)^2}{\sigma_w^2}\right]. \tag{2.1}$$

Here $w_0$ is a baseline fitness.

The level of the epigenetic state, and hence the phenotype, is determined by inheritance from the previous generation and an environmentally induced effect, as follows:

$$y_{t+1} = hy_t + m_t + d_t. \tag{2.2}$$

The evolvable parameter $h$ models the degree of epigenetic resetting (i.e. $0 =$ complete resetting, $1 =$ no resetting), $m_t$ is a maternal environmental effect on the epigenetic state and $d_t$ represents developmental noise. We assume that the latter is Gaussian with mean zero and variance $\sigma_d^2$, independent of the environmental and epigenetic state:

$$d_t \sim N(0, \sigma_d^2). \tag{2.3}$$

We model the maternal effect as a linear reaction norm with respect to the mother's *perceived* environmental state $x_t + \varepsilon_t$, where the maternal error $\varepsilon_t$ is assumed to be Gaussian with mean zero and variance $\sigma_\varepsilon^2$:

$$m_t = m_0 + m_1(x_t + \varepsilon_t) \tag{2.4a}$$

and

$$\varepsilon_t \sim N(0, \sigma_\varepsilon^2). \tag{2.4b}$$

So $m_0$ is the baseline maternal effect if the mother does not respond to her environment, and $m_1$ describes how much the maternal effect changes for a change in one unit of the environmental state.

Given maternal marks $y_t$, the distribution of marks among their offspring is then given by the Gaussian

$$H(y_{t+1}|y_t) = (2\pi\sigma_H^2)^{-1/2}\exp\left[-\frac{1}{2}\frac{(y_{t+1} - hy_t - \bar{m}_t)}{\sigma_H^2}\right], \tag{2.5}$$

where

$$\bar{m}_t = m_0 + m_1 x_t \tag{2.6a}$$

and

$$\sigma_H^2 = m_1^2\sigma_\varepsilon^2 + \sigma_d^2. \tag{2.6b}$$

Assuming the population distribution of marks in year $t$ is Gaussian with mean $\mu_t$ and variance $\sigma_t^2$, i.e.

$$G_t(y_t) = (2\pi\sigma_t^2)^{-1/2}\exp\left[-\frac{1}{2}\frac{(y_t - \mu_t)^2}{\sigma_t^2}\right], \tag{2.7}$$

then the distribution in the next year is also Gaussian

$$G_{t+1}(y_{t+1}) = \bar{w}_t^{-1}\int H(y_{t+1}|y_t)w(y_t)G_t(y_t)\,\mathrm{d}y_t. \tag{2.8}$$

The mean fitness $\bar{w}_t$ normalizes the distribution and is given by

$$\bar{w}_t = \int w(y_t)G_t(y_t)\,\mathrm{d}y_t = w_0\sqrt{\alpha}\exp\left[-\frac{1}{2}\frac{(\mu_t - x_t)^2}{\sigma_w^2 + \sigma_t^2}\right], \tag{2.9}$$

where

$$\alpha = \frac{\sigma_w^2}{\sigma_w^2 + \sigma_t^2}. \tag{2.10}$$

The recursions for the mean and variance of the marks are given by

$$\mu_{t+1} = h\alpha\mu_t + h(1 - \alpha)x_t + \bar{m}_t \tag{2.11a}$$

and

$$\sigma_{t+1}^2 = h^2\alpha\sigma_t^2 + \sigma_H^2. \tag{2.11b}$$

The long-term growth factor (i.e. geometric mean fitness) of the population is the expected value (operator $E$, taken over the whole time series) of the log-mean fitness:

$$\lambda = E[\ln(\bar{w}_t)] = \ln(w_0) + \frac{1}{2}\ln(\hat{\alpha}) - \frac{1}{2}\frac{E[(\mu_t - x_t)^2]}{\sigma_w^2 + \hat{\sigma}^2}. \tag{2.12}$$

The hats indicate that the equilibrium value of the epigenetic mark variance recursion (2.11b) should be used. This is given by

$$\hat{\sigma}^2 = \frac{1}{2}(\sigma_H^2 - (1 - h^2)\sigma_w^2 + [(\sigma_H^2 + (1 - h^2)\sigma_w^2)^2 + 4h^2\sigma_H^2\sigma_w^2]^{1/2}). \tag{2.13}$$

Note that when $h = 0$, $\Rightarrow \hat{\sigma}^2 = \sigma_H^2$.

### (b) The environment

To derive the conditions that favour incomplete epigenetic resetting (i.e. $h > 0$), we need to make assumptions about
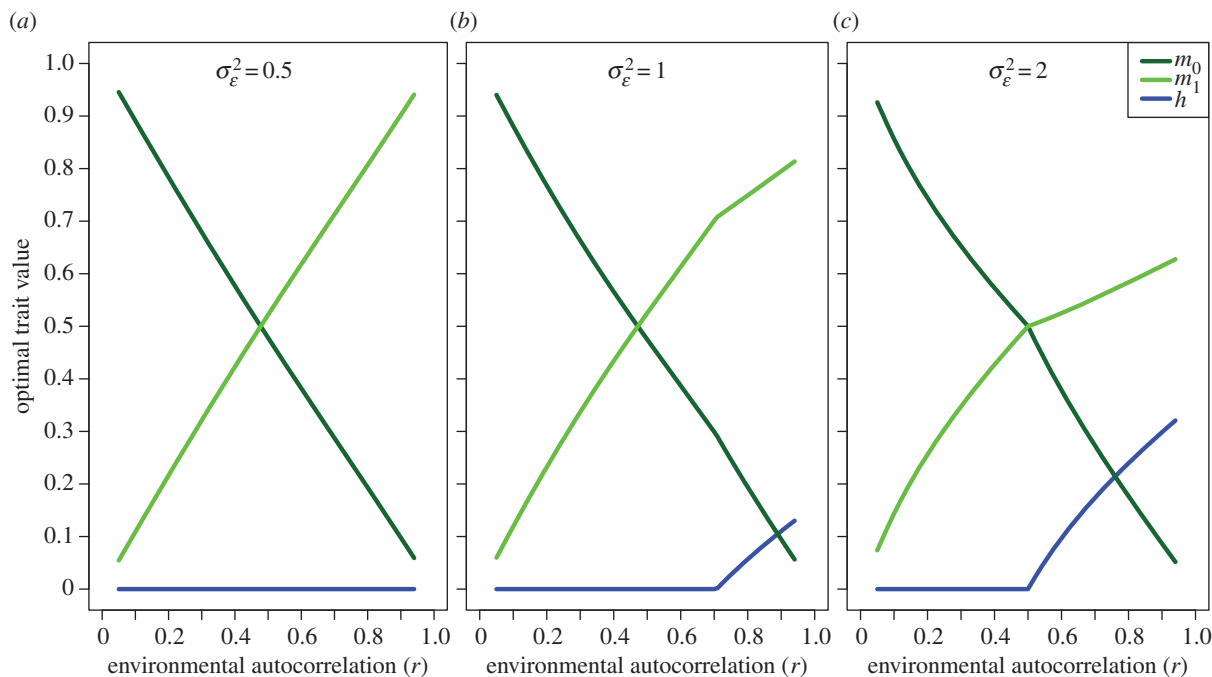
**Figure 1.** Conditions that select for maternal effects and incomplete resetting. Incomplete resetting is higher when both the environmental autocorrelation and variance in environmental maternal effects are high. Other parameter values: $\sigma_w^2 = 1$, $\sigma_e^2 = 2$, $\sigma_d^2 = 0.5$. (Online version in colour.)

the dynamics of the environmental state $x_t$. We assume that the environment is autocorrelated according to a first-order autoregressive model, where $\mu_x$ is the long-term average environmental state, $r$ ($0 \leq r < 1$) is the degree of correlation between successive generations, and $e_t$ is a Gaussian error term

$$x_{t+1} = rx_t + (1-r)\mu_x + e_t \qquad (2.14a)$$

and

$$e_t \sim N(0, \sigma_e^2). \qquad (2.14b)$$

This standard model has the following long-term properties:

$$E(x_t) = \mu_x, \qquad (2.15a)$$

$$\text{var}(x_t) = \frac{\sigma_e^2}{(1-r^2)} \qquad (2.15b)$$

and $\qquad \rho(x_{t+1}, x_t) = \dfrac{\text{cov}(x_{t+1}, x_t)}{\text{var}(x_t)} = r. \qquad (2.15c)$

Here $\rho$ is the autocorrelation between the environmental states of subsequent generations. We can choose $\mu_x$ and $\sigma_e^2$ such that in practice $x$ and $y$ are never negative, which is appropriate for many epigenetic mechanisms, including DNA methylation. Note that $r = 0$ implies that the environments of subsequent years are uncorrelated.

## (c) Main results

The mean square term in (2.12) can be completed by solving the recursions (2.11a) and (2.14a) for $\mu_t$ and $x_t$, squaring their difference and taking expectations. Plugging the result in (2.12) gives

$$\lambda = \ln(w_0) + \frac{1}{2}\ln(\hat{\alpha})$$
$$-\frac{1}{2}\sigma_e^2 \frac{A(B^2 r/(1-r^2) - 2B - r) + B^2/(1-r^2) + 1}{(\sigma_w^2 + \hat{\sigma}^2)(1 - A^2)(1 - Ar)}$$
$$-\frac{1}{2}\left(\frac{m_0 - C}{1 - A}\right)^2, \qquad (2.16)$$

where

$$A = h\alpha, \qquad (2.17a)$$

$$B = h + m_1 - r \qquad (2.17b)$$

and $\qquad C = (1 - h - m_1)\mu_x. \qquad (2.17c)$

We can now find the equilibrium values of the evolvable parameters $h$, $m_0$ and $m_1$ by maximizing $\lambda$.

The optimal baseline maternal effect is given by

$$m_0^* = C = (1 - h - m_1)\mu_x. \qquad (2.18)$$

Substituting equation (2.18) into (2.16) eliminates the last term on the right, and we continue working with the truncated formula.

Selection favours incomplete resetting ($h > 0$) if $\partial\lambda/\partial h > 0$ when evaluated at $h = 0$. It turns out that

$$\left.\frac{\partial\lambda}{\partial h}\right|_{h=0} = \frac{(r - m_1)\sigma_e^2(m_1^2\sigma_\varepsilon^2 + rm_1\sigma_w^2 + \sigma_d^2)}{(1-r^2)(m_1^2\sigma_\varepsilon^2 + \sigma_w^2 + \sigma_d^2)^2}. \qquad (2.19)$$

Note that all factors except for $(r - m_1)$ are always positive. Thus, incomplete resetting evolves if $r > m_1$. The next step is therefore to ask if selection on $m_1$ favours $r > m_1$, and this can be checked by inspecting the sign of $\partial\lambda/\partial m_1$ evaluated at $h = 0$ and $m_1 = r$:

$$\left.\frac{\partial\lambda}{\partial m_1}\right|_{h=0, m_1=r} = \frac{-r\sigma_e^2(r^2\sigma_\varepsilon^2 - \sigma_e^2 + \sigma_w^2 + \sigma_d^2)}{(r^2\sigma_\varepsilon^2 + \sigma_w^2 + \sigma_d^2)^2}. \qquad (2.20)$$

This shows that selection favours lower values of $m_1$ at $h = 0$ and $m_1 = r$ when the second factor in the numerator is positive, i.e. when

$$r^2\sigma_\varepsilon^2 > \sigma_e^2 - \sigma_w^2 - \sigma_d^2. \qquad (2.21)$$

Thus, selection favours incomplete resetting if the environmental autocorrelation and the maternal error rate are sufficiently high, as measured by the product $r^2\sigma_\varepsilon^2$ (figure 1). Moreover, this condition is more likely to hold when selection is weak (higher $\sigma_w^2$) and developmental
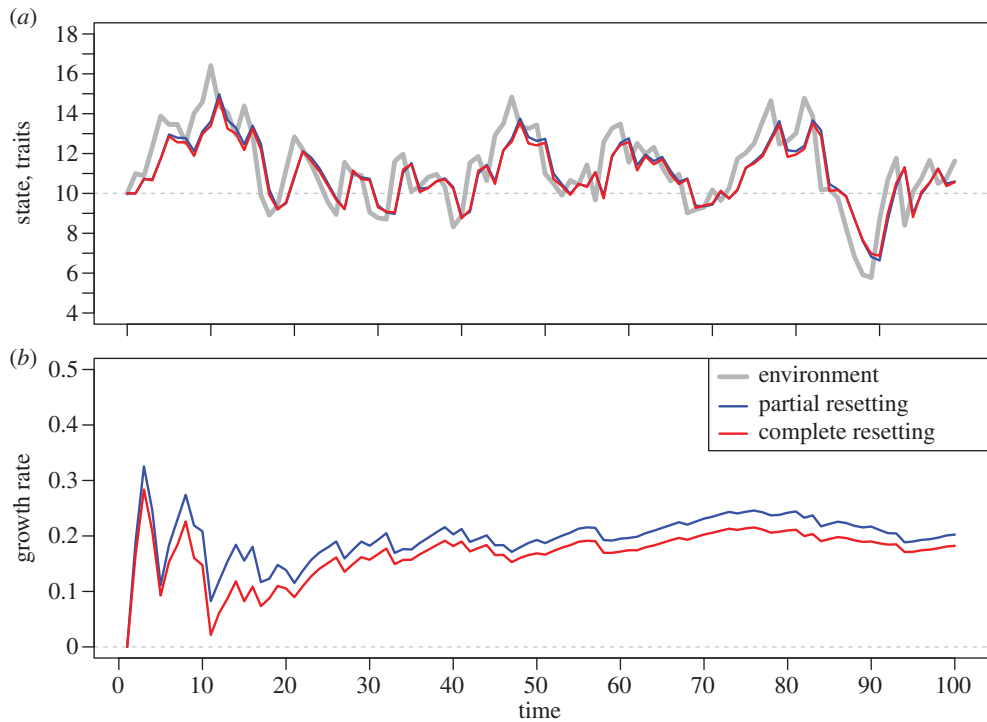
**Figure 2.** (a) Example of how the epigenetic state (and trait) tracks the environment under complete (red) and partial (blue) resetting. (b) The long-term population growth rate is higher for partial resetting. Parameter values are the same as in figure 1c with $r = 0.8$. (Online version in colour.)

noise is not too small relative to the environmental fluctuations (i.e. $\sigma_w^2 + \sigma_d^2 \approx \sigma_e^2$). Figure 2 shows how the optimal partial resetting and complete resetting follows the environmental variation and the long-term fitness differences (expected population growth rate) between the two strategies.

## 3. Individual-based simulations

To complement and verify the analytical results, we make use of individual-based simulations to model the evolution of incomplete resetting in either a spatially or a temporally heterogeneous environment.

### (a) Phenotypes, inheritance and selection

We model a population of asexual haploid organisms with two possible phenotypes, $z = 0$ and $z = 1$. Each individual has an epigenetic state, $y$, which is a continuous variable. In contrast to the analytical model, the epigenetic state is translated into one of two discrete phenotypes; if an offspring's epigenetic state $y$ exceeds a threshold value, the offspring develops phenotype 1 and otherwise it develops phenotype 0. We fix the threshold to zero, such that negative values of $y$ produce phenotype 0 and positive values produce phenotype 1. This implies that the state will decay in the absence of environmentally induced effects if there is incomplete resetting, which can be interpreted as (gradual) reversal to a default epigenetic state (e.g. of a target gene(s) that makes phenotype determination random (i.e. $y = 0$)). Conversely, under complete resetting, offspring phenotype would be dictated by the environmentally induced effect on the epigenetic state. Unlike the analytical model, the environment takes one of two discrete states ($E \in \{0,1\}$). If the individual's phenotype matches the environment (i.e. if $z = E = 0$ or $z = E = 1$), its viability is 1, while if its phenotype does not match the

environment (i.e. if $z = 1$ and $E = 0$ or $z = 0$ and $E = 1$), its viability is reduced to $1 - s$.

The epigenetic state transmitted to the following generation is determined by the extent of incomplete epigenetic resetting following sequestration of germ cells from somatic cells ($h$), and environment-dependent modification of the epigenetic state, $m_i$ (where $i = 0$ or 1). These variables are assumed to be determined by three stably inherited (genetic) loci. As in the analytical model, the epigenetic state of offspring is a function of the epigenetic state of the mother, the degree of epigenetic resetting, and a maternal effect that depends on the mother's environment with an added developmental noise (equation (2.2); electronic supplementary material, figure S1a).

In the simulation model, we also consider two alternative scenarios. In the first, parental environment-dependent modification occurs before resetting and, in the second, offspring environment-dependent modification occurs after epigenetic resetting (electronic supplementary material, figure S1b,c). Possible mechanisms that could result in either of these scenarios have recently been described in the literature (see Introduction).

### (b) The environment

We construct simulations in a spatially or temporally heterogeneous environment. In the spatial model, the population is sub-divided into smaller patches that are connected by individual dispersal at rate $D$. The proportion of patches of type 0 is $q$ and that of type 1 is $1 - q$. We consider a range of dispersal rates when patch types are equally common and we also investigate how incomplete resetting evolves when patch types occur at different frequencies. The temporal environment is cyclical with a period $2n$, such that the environment is in state 0 for $n$ breeding cycles followed by $n$ breeding cycles where the environment is in state 1.
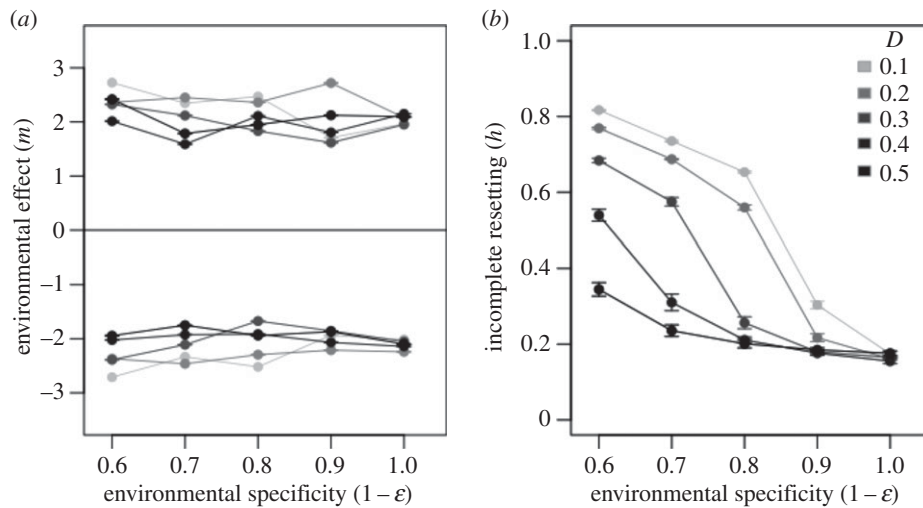
**Figure 3.** Evolution of (*a*) direct environment effects and (*b*) incomplete epigenetic resetting in a spatially heterogeneous environment when the two environments are equally frequent. Means and s.e. are calculated from 10 replicates where each data point is the average of the last 10 000 generations of the simulation. Different levels of offspring dispersal (*D*) are delineated by the different shading of the lines (see legend). The environment specificity $(1 - \varepsilon)$ is set such that a value of 0.6 means an individual receives the level of the environmental effect ($m_i$) matching its environment (i.e. $m_1$ when $E = 1$) with a probability of 0.6.

The environmental specificity of the inducing factor is determined by the parameter, $\varepsilon$, which is analogous to $\sigma_\varepsilon^2$ in the analytical model. When an individual is in environment 0, the epigenetic state is affected by the value at the locus $m_0$ with probability $1 - \varepsilon$, otherwise it is affected by the value of the locus $m_1$ (and vice versa for individuals in environment 1). Further details on the models and their parameter settings can be found in the electronic supplementary material.

## (c) Main results

The general patterns are similar for the three different timings of epigenetic resetting relative to environmental induction, although the baseline level of incomplete resetting evolves to a higher level when resetting occurs after, rather than before, phenotype determination (electronic supplementary material, figures S2 and S3). In what follows, we therefore refer only to results for the version that is analogous to the analytical model (i.e. $y_{t+1} = hy_t + m_t + d_t$) and provide results for the other scenarios in the electronic supplementary material. In the electronic supplementary material, we also give examples of simulation runs to demonstrate how $h$, $m_0$ and $m_1$ evolve over time (electronic supplementary material, figures S4 and S5).

In the spatially heterogeneous environment with equal patch-type frequencies, we find that incomplete resetting evolves when both the rate of dispersal and the specificity of environmental maternal cues are low (figure 3). Similar results occur when patch types occur at different frequencies. However, when one environment is uncommon and the specificity of environmental (maternal) cues is low, the system evolves to produce a single phenotype (i.e. both $m_0$ and $m_1$ are positive) and as a consequence there is no selection on epigenetic resetting (figure 4).

In the cyclical environment, incomplete resetting is favoured when the environment remains stable for long periods and the specificity of the environmental maternal cue is low (figure 5). However, we also find that incomplete resetting is favoured at a period of only four generations (figure 5). We explain this special case in the electronic supplementary material (figure S6).

## 4. Discussion

There is increasing empirical evidence for transgenerational epigenetic inheritance in microbes, plants and animals. This has generated substantial controversy, not the least because it is unclear whether such inheritance could ever be adaptive [41]. Our models show that incomplete resetting between generations can evolve when the correlation of environmental states across generations is high and the accuracy of environmental cues is low. Here, we explain the rationale for these results and how they compare to previous models, and discuss how applicable the theory is to natural systems.

The analytical model extends results from a recent model of optimal introduction and transmission of variants in variable environments [38]. Our results show that incomplete resetting of epigenetic states in germ cells can be favoured when the environmental autocorrelation is high and (maternal) environmental cues are unreliable. These results were corroborated by individual-based simulations where the phenotypes were discrete and developed according to a threshold model; incomplete resetting evolved in environments that changed infrequently relative to generation time and when environmental (maternal) effects showed low environmental specificity.

Our results can be interpreted by considering how passive transmission of epigenetic states across generations contributes to fitness. During periods of environmental stability, incomplete resetting protects against mismatched phenotypes that would otherwise result from responses to imperfect environmental or maternal cues. But incomplete resetting also has negative fitness consequences. This can be illustrated by comparing the fitness consequences of different resetting strategies following environmental change. Whereas complete resetting will tend to result in a suboptimal phenotype only in the first generation following environmental change (because of a mismatched maternal effect), incomplete resetting can cause the wrong phenotype to develop in two or more consecutive generations (see also [36]). Thus, when environmental autocorrelation is high and cues are inaccurate, the fitness benefits of avoiding mismatched phenotypes (through incomplete resetting of epigenetic marks) outweigh
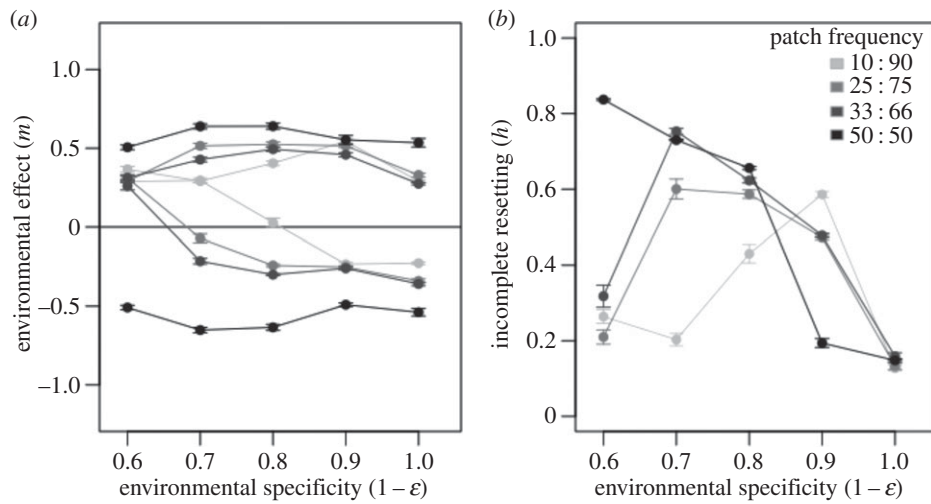
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**Figure 4.** Evolution of (a) direct environment effects and (b) incomplete epigenetic resetting in a spatially heterogeneous environment with different proportions of patch types 0 and 1. Means and s.e. are calculated from 10 replicates where each data point is the average of the last 10 000 generations of the simulation. Different patch frequencies are delineated by the different shading of the lines (see legend). Dispersal probability is 0.2 and the environment specificity $(1 - \varepsilon)$ is set such that a value of 0.6 means an individual receives the level of the environmental effect ($m_i$) matching its environment (i.e. $m_1$ when $E = 1$) with a probability of 0.6.
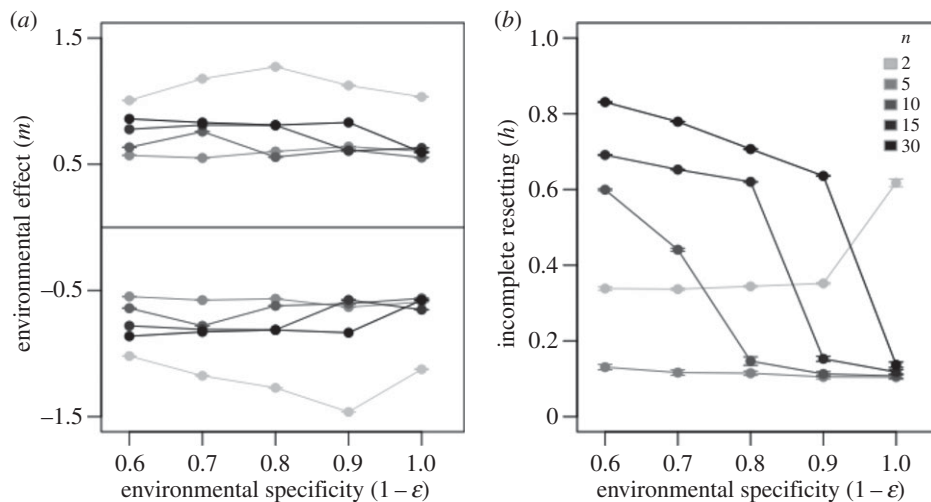


**Figure 5.** Evolution of (a) direct environment effects and (b) incomplete epigenetic resetting in a temporally cyclical environment. Means and s.e. are calculated from 10 replicates where each data point is the average of the last 10 000 generations of the simulation. Different environmental periods (2n) are delineated by the different shading of the lines (see legend). As explained above, the environment specificity $(1 - \varepsilon)$ is set such that a value of 0.6 means an individual receives the level of the environmental effect ($m_i$) matching its environment (i.e. $m_1$ when $E = 1$) with a probability of 0.6.

the fitness benefits of rapidly adjusting the phenotype when the environment changes. The opposite is true when environmental autocorrelation is low and environmental or maternal cues reliably predict the environment of the next generation. In other words, the selective advantage of incomplete resetting depends on the statistical structure of the environment that dictates to what extent epigenetic inheritance carries information [24,38,39]. Furthermore, the same reasoning also explains why incomplete resetting is more likely to evolve when the strength of selection against mismatched phenotypes is weak relative to the rate of environmental change.

A combination of incomplete resetting and maternal induction should be manifested as environmental effects on epigenotype and phenotype that persists over several generations, the magnitude of which may depend on the maternal or offspring environment, or both. Such effects are increasingly observed in animals and, in particular, plants (reviews in [4,5,17,19,42]), where studies of experimental lines suggest that induced patterns of DNA methylation are readily inherited [11]. Similarly, in mammals, DNA sequences can resist

reprogramming [43,44], and the extent of demethylation is regulated by the methylation machinery [45,46]. Thus, although we often expect transgenerational epigenetic inheritance to be maladaptive (or fitness neutral), the extent of resetting could evolve in response to selection. Prime candidates for adaptive incomplete resetting are organisms that live in environments where the rate of change is slow relative to generation time and reliance on environmental cues is constrained or costly. This may apply to some plant species during ecological succession, in species that undergo population cycles due to colonization and extinction dynamics, or in highly sedentary animals living in seasonal environments. The same logic may also explain instances of transgenerational stability of environmentally induced phenotypes in more mobile animals, such as tolerance of *Daphnia* to seasonal algal blooms [47]. Notably, many studies designed to test for local adaptation, phenotypic plasticity or even maternal effects will fail to detect incomplete resetting as those experiments typically do not investigate multi-generational responses. The prevalence of incomplete resetting in putative selective regimes is therefore impossible

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to assess with current data. We also suggest that incomplete resetting may be a transient evolutionary stage that connects environmental induction of adaptive variation and its genetic accommodation [48,49]. Under this scenario, incomplete resetting may initially be favoured by selection but would eventually be replaced by within-generation plasticity after, for example, an innovation in how cues are assessed.

That incomplete resetting of epigenetic states is only expected to be favoured when the environment fluctuates slowly relatively to generation time may seem surprising considering that transgenerational epigenetic inheritance is often argued to be adaptive when fluctuations occur on the time scale of a small number of generations (e.g. [20,21,25, 32,33]). The difference arises because previous models have typically contrasted more or less stable passing of epigenetic variants (i.e. epialleles) between generations with within-generation plasticity or genetic inheritance [32,33,36,37]. For example, in the model of Jablonka et al. [32], the environment changed within generations, between the induction and selection stage, so that highly responsive phenotypes did worse in variable environments. Selection against plasticity directly results in transgenerational stability of phenotypes in this model since the adult always passes on its (sometimes acquired) phenotype to the offspring unchanged. Other models that are sometimes couched in terms of epigenetic inheritance have considered optimal phenotypic switching or bet-hedging (e.g. [50]). Our approach is different because we explicitly modelled the joint evolution of plasticity and inheritance, which can result in partial inheritance of acquired states. As with maternal effects [39,40,51–53], the adaptive value of this environment-dependent heredity depends on the statistical relationship between environmental fluctuations and generation time [38].

To gain further insights into these phenomena, it may be important to consider more mechanistic details. For example, the epigenetic response to an environmental stimulus may depend on the initial epigenetic state, which perhaps could make incomplete resetting favoured under a broader range of environments [54]. Our model is also very simple in that it deals with asexual haploid organisms. It is likely that sexual reproduction will be important as both parents can contribute to the epigenetic state of the offspring. Because sexes may differ in their tendency to disperse, this could select for parent-of-origin-specific parental effects and incomplete resetting [39,53]. Finally, as in all models, we constrained the possible solutions to the problem posed by the environment. For example, dispersal did not evolve in the spatial simulation model, yet conditions favouring incomplete resetting may instead select for increased dispersal, which in turn would relax selection on epigenetic inheritance.

In summary, we show that incomplete epigenetic resetting can adaptively coevolve with plasticity or maternal effects in heterogeneous environments. This may contribute to empirical observations of cumulative or persistent trans-generational epigenetic inheritance spanning several generations in plants and animals. However, our results suggest that adaptive incomplete resetting should be restricted to situations where environmental change is infrequent relative to generation time and direct environmental cues are unreliable. How often these conditions are met in nature, and whether or not incomplete resetting has evolved in response to these conditions, remain open questions.

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