Evolutionary Simulations of Maternal Effects in Artificial Developmental Systems

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Abstract. Maternal influence on offspring goes beyond strict nuclear (DNA) inheritance: inherited maternal mRNA, mitochondria, caring and nurturing are all additional sources that affect offspring development, and they can be also shaped by evolution. These additional factors are called maternal effects, and their important role in evolution is well established experimentally. This paper presents two models for maternal effects, based on a genetic algorithm and simulated development of neural networks. We extended a model by Eggenberger by adding two mechanisms for maternal effects: the first mechanism attempts to replicate maternal cytoplasmic control, while the second mechanism replicates interactions between the fetus and the uterine environment. For examining the role of maternal effects in artificial evolution, we evolved networks for the odd-3-parity problem, using increasing rates of maternal influence. Experiments have shown that maternal effects increase adaptiveness in the latter model.

1 Introduction

Traditionally, when considering traits' variation in organisms, sources for variation are divided into genetic contributions and effects due to the environment. Recently, another important source for variation has been increasingly considered, that occurs when the environment for the organism is provided by another (usually con-specific) phenotype. Indirect genetic effects [7] occur when this environmental influence is genetically based, that is, the genes of an individual affect another individual indirectly through the provided environment. Among these effects, maternal effects, that is, effects that occur between mother and offspring are the most extensively studied. Maternal effects are ubiquitous in metazoans and also found extensively in plants. Besides supplying half of the DNA to their offspring, mothers additionally contribute essential factors for their early development, nutrition, rearing, and cultural conditioning [6]. For instance, early developmental stages in all metazoans are under exclusive control of maternal gene products deposited in the egg during oogenesis (egg formation). Even after the transition to zygotic gene regulation, products resultant from early maternal cytoplasmic control still take important roles in development. Additionally,

in mammals, interaction between the placenta and the fetus can be an important influence. All of these factors can be additional sources for affecting the offspring's phenotype in addition to strict nuclear inheritance. A summary of the major maternal effects are shown in figure 1.

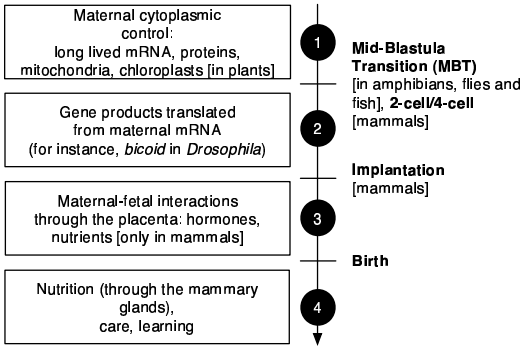

Fig. 1. Summary of the maternal contributions to offspring development.

Maternal effects can influence evolution significantly in two ways, both producing unusual outcomes. First, contrary to what is expected from standard Mendelian genetics, traits in the mother and in the offspring may be negatively correlated [5]. The end result from this is that selection for a specific trait may in fact produce a temporally reversed response, that is, selection for a larger trait in mothers would produce offspring with smaller traits, and selection for smaller traits would produce larger traits. This was observed experimentally by Falconer [3], who performed artificial selection experiments for larger litter size in mice: In his experiments, selection for larger litter size resulted in mothers having larger litters, but that developed into smaller adults; in contrast, mice from smaller litters would grow into bigger adults, when compared to the ones developed from the larger litters. Falconer inferred that this should be due to increased competition for milk in the larger litters, that would create smaller adults due to less available milk from their mothers.

Second, maternal effects can create time lags in selection response, generating a kind of "evolutionary momentum", where a trait may continue evolving even if selection ceases. Kirkpatrick and Lande [5] created a quantitative genetics model, taking into account maternal inheritance, where this effect is observed. In their model, evolutionary momentum occurs whenever traits between mother and offspring are related, with either a trait present in the mother directly affecting the same trait in offspring, or indirectly through other traits. The direction of evolutionary momentum, or how the affected trait evolved after selection ceases, depends on whether the traits are negatively or positively correlated.

In this article, we introduce two models for maternal effects, both focusing on how these effects occur at the molecular level, i.e. due to exchange of gene products between mother and offspring, and resultant affected gene regulation (Figure 1, boxes (1) and (3)). The first model attempts to replicate maternal cytoplasmic influence in the early stages of metazoan development, while the second models the exchange of chemicals between the mother and the fetus in mammals. For this, we adopted a developmental model by Eggenberger [2], that uses simulated gene regulation and cell communication for generating neural networks. Coupled with a genetic algorithm, we then evolved networks for solving the odd-3-parity problem, with increasing maternal influence in both models.

2 The models

2.1 Overview

A conceptual overview of both models, compared with the one based on the standard evolutionary perspective, is shown in figure 2. In these models, both mother and offspring undergo development, that maps their genotype to their final phenotype. There are two sources accounting for variation in the final offspring phenotype, the first being the standard maternal genetic contribution, and the second being an additional mechanism, depending on the model.

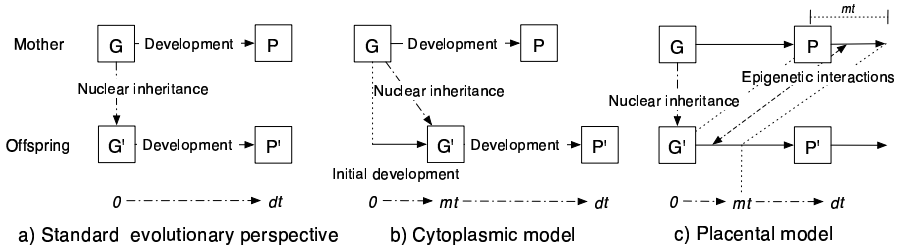

Fig. 2. Conceptual overview. (a) Standard evolutionary perspective. (b) Cytoplasmic model. (c) Placental model.

The first model attempts to replicate maternal cytoplasmic control as it occurs in the early stages of development in all metazoans. During metazoan oogenesis, the mother places mRNA and proteins in the egg, that directs early development until transcription from the zygote (the fertilized egg) starts. The stage where this occurs depends on the species, being the Mid-Blastula Transition (MBT) stage in amphibians, flies and fish, and the 2-cell or 4-cell stage in mammals. Depending on the species, in these early stages, there can be a significant interaction between the maternal gene products and the zygote, but there are at least some species where maternal control is exclusive. In these species, the

eggs are able to develop normally in the early stages, even if the sperm and zygotic nucleus are artificially removed. In a similar way, we decided to model this early maternal control by using the mother's genotype as the exclusive source for the offspring's early development. After mt time steps are reached, the real offspring genotype is used for resuming development until dt time steps, where it is considered the final phenotype. Using the maternal genome directly, as it occurs in this model, is a significant abstraction from the way real cytoplasmic control works, because maternal mRNA, responsible for early development, is a product from maternal genes, and not the maternal genes themselves. We believe that this abstraction is still able to preserve the two essential points for this kind of maternal influence, namely: 1) Early development is controlled by maternal genes; 2) It is mainly unidirectional, occurring from the mother to the offspring.

The second model attempts to model interactions between the mother, the growing fetus and the placenta, as it occurs in mammals. In mammals, placenta development occurs after the embryo is formed, and is regulated by both the mother and the embryo. Placental influence works both ways, not only affecting the embryo, but also affecting the mother herself — for instance, by adapting her morphology to nurture adequately after giving birth. Influence in fetus development has been extensively studied in embryo transfer experiments: for instance, Cowley [1] performed embryo transfers between two different mice strains, one significantly larger than the other. In his experiments, mice transfered into the larger strain were always able to grow larger, regardless of their own genotype. An example of influence in the mother are the hormones oestrogen and prolactin, produced by the placenta, and that are responsible for preparing the breasts for milk production in humans. For the sake of simplicity, in our model we decided not to add the placenta as a mediator, and instead to allow the mother and offspring to influence each other directly. In our model, therefore, development occurs concurrently for the mother and offspring; during offspring development, the mother's development is resumed, and epigenetic interactions occur between them for mt time steps. This still allows for changes both in the mother and offspring as described before, without having to model an additional entity.

2.2 Development and evolution

For implementing the models described before, we used a simulated developmental model for neural networks, based on gene regulation and cell communication. Our developmental model is based on a previous one by Eggenberger [2]. We used boolean neural networks with thresholds as either 0 or 1, and the connections being either -1 or 1. Neurons are activated if the sum of the values on their incoming connections is above their threshold. Development proceeds in a rectangular grid, each slot possibly having a neuron, depending on the experiment settings. Each neuron contains a copy of the same genome. Chemicals are generated by gene activity inside each neuron, and diffuse through the grid. Although all neurons contain the same genome, different parts of the genome may be activated on each neuron, due to interactions through chemical diffusion.

All the simulated substances contain a real valued *geom* parameter, with possible values ranging between 0 and 1. This *geom* parameter is used for describing the geometric properties of the substance (for instance, as an abstraction for protein structure), and for attributing a binding between two substances. This is used, for instance, for computing the binding of substances to regulatory regions, and also between Cell Adhesion Molecules (CAMS) as it will be explained later. The affinity between two substances $affinity(geom_1, geom_2)$ is computed by $e^{-|geom_2 - geom_1|}$, where $geom_1$, $geom_2$ are the *geom* values for the two substances. If this affinity is 1 for any two given substances, then they match evenly, while the minimum value, $\frac{1}{e}$, represents no match at all.

The genome is real-valued, and organized in an operon-like structure with structural and regulatory regions. Structural regions are responsible, if activated, for generating chemical substances; regulatory regions are used for activating the associated structural regions, depending on the substance's concentration in the cell. A sample structure is shown in figure 3 a).

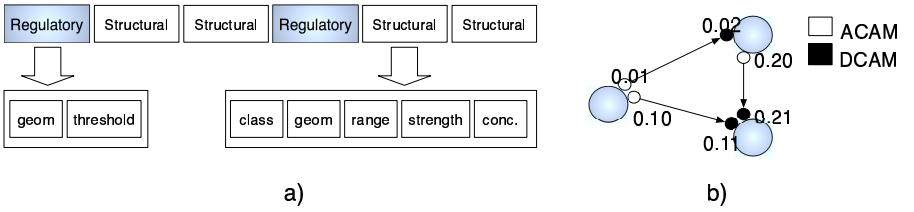

Fig. 3. a) Sample genome structure. In the structural regions, **class** indicates the kind of substance that is produced if the gene is activated, while **geom** represents the geometry of the generated substance. **Range** and **strength** are only expressed in the CAMs: **range** indicates the search range for the CAMs, while **strength** indicates the strength of the synapse (-1 if less than 0.5, 1 if greater than 0.5). **Concentration** indicates the amount produced on each time step, if the gene is activated. As for the regulatory regions, **geom** is used for template matching with the molecules, while **threshold** represents the minimum required affinity for activating the structural gene. b) Neurons connecting to each other. Due to gene regulation, each neuron expresses CAMs in their surfaces, with different **geom** values. Connections are established between (ACAM, DCAM) pairs that have the strongest $affinity(geom_1, geom_2)$.

On each developmental time step, substances inside the neuron compete for binding in the regulatory regions of the genome. The one with the highest affinity to the corresponding regulatory part successfully binds to it. If their concentration times the affinity is above the threshold, then the corresponding structural genes are activated. One regulatory region controls several structural regions, with the number of structural regions per regulatory parts fixed, and defined as a parameter for the experiments. Structural genes can produce three kinds of substances: transcription factors remain inside the neuron, signaling molecules diffuse out of the neuron, and CAMs are used for connecting neurons with

synapses. Diffusion is simulated by using a discrete version of Fick's law, with the same diffusion and evaporation coefficients for all the substances. The diffusion equation is:

$$c(x, y, t+1) = (1 - 4D - E) \cdot c(x, y, t) + D \cdot (c(x-1, y, t) + c(x+1, y, t) + c(x, y-1, t) + c(x, y+1, t)), \quad (1)$$

with $c(x, y, t)$ the concentration of a substance at position (x, y) in the grid at time t, D the diffusion rate, and E the evaporation rate. Concentrations at the boundaries are assumed to be 0. CAMs are expressed at the surface of each neuron, and used for connecting them. Besides the *geom* parameter, they also contain a *strength* and a *range*. They are further divided into two different kinds: ACAMS (axom) and DCAMS (dendrite). If two cells express CAMs with enough affinity between them, then a connection is established. On each time step, neurons with expressed ACAMS will search on their neighborhood for neurons with suitable DCAMs. If the affinity is high enough, a connection will be established between the pair with the highest affinity, from the ACAM to the DCAM. The search range for each neuron is encoded in the *range* parameter, as a percentage of the whole grid size. *strength* specifies the strength of the connection. An example is shown in figure 3 b).

For simulating evolution, we use a genetic algorithm coupled with the developmental model defined before. No crossover operation was applied, only reproduction and mutation were used. Therefore, the individuals between subsequent generations are always connected by a reproduction operation, and alternate roles between mother and offspring in each generation: that is, an individual in generation m connected to another individual in generation $m + 1$ takes the maternal role for that individual in generation $m + 1$.

Figure 4 shows how both models are implemented. For simulating early cytoplasmic control, development occurs in two discrete stages: in the first stage, the maternal genome is used exclusively in all the cells of the grid until mt time steps are reached. Afterward, the offspring's genome replaces the previous genome in all the cells and guides the remaining development. For the placental model, development for the mother is resumed, and occurs concurrently with the offspring, during mt time steps. During this stage, chemicals are exchanged between the mother and offspring, on each corresponding cell in both grids, using a mD exchange rate. After this stage, development occurs for the offspring as usual, without any further maternal influence.

3 Experiments and results

Using this model, we evolved networks for the 3-odd-parity problem. The solution is defined as a neural network with at least 3 inputs, that outputs *true* whenever the number of *true* inputs is odd. All the grids were initialized with a neuron configuration sufficient for this problem: 3 input neurons, 5 hidden neurons (3 with threshold 0, 2 with threshold 1), and 1 output neuron.

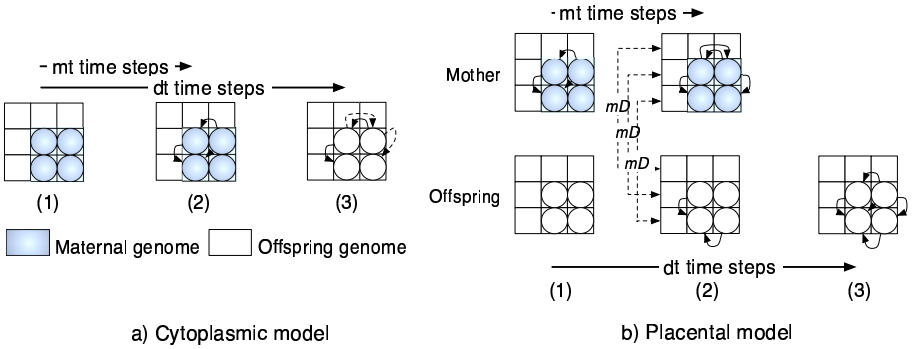

Fig. 4. Diagram for both models. In both models, **(1)** represents the initial stage, **(2)** the stage where until maternal influence occurs, and **(3)** the final stage. Please note that in the placental model, all maternal cells exchange chemicals with their corresponding offspring cell, although this is only shown for the the leftmost column.

A fitness function based on the number of wrong outputs did not produce a good performance so we used a fitness function used by Gruau in [4]. It is defined by:

$$f(out_{eval}) = \frac{I(out_{right}, out_{eval})}{H(out_{right})}, \tag{2}$$

where out_{eval} is the output vector of the evaluated network and out_{right} is the expected correct output vector for the problem. $I(X, Y)$ is the mutual information between X and Y, and $H(X)$ is the information entropy of X:

$$I(X,Y) = \sum_{x=0}^{1}\sum_{y=0}^{1} P_{XY}(x,y) \cdot log_2\left(\frac{P_{XY}(x,y)}{P_X(x) \cdot P_Y(y)}\right), \tag{3}$$

$$H(X) = \sum_{i=0}^{1} P_X(i) \cdot log_2(P_X(i)), \tag{4}$$

with $P_X(x)$ as the probability of $X = x$, and $P_{XY}(x, y)$ as the joint probability of $X = x$ and $Y = y$. This fitness function is defined in the range $[0, 1]$, with 1 as the best fitness. Due to using mutual information, both the correct output and its negation will have the same best fitness.

We conducted three sets of experiments: one using the cytoplasmic model, and two using the placental model with two different mD values (0.2 and 0.8). For understanding the role of maternal effects in network development, in each set we conducted experiments with dt fixed at 30 time steps, and used increasing values of mt. The used mt values correspond to periods of initial maternal influence for 0%, 10%, 30%, 50%, 70% and 100% of the total developmental time (mt/dt). Each case was conducted 10 times, with different random seeds in each run. The

experiments were conducted with the ECJ (Evolutionary Computation in Java) package. Evolution was conducted for 300 generations with a population size of 600. Roulette wheel selection was used, and selected individuals for reproduction had a 50% chance of being mutated. The mutation operator, if it was applied, generated a new random value in only one slot (chosen at random) in the genome. The genomes used in the experiments contained 6 regulatory regions, with each region having 5 structural regions attached. The grid size was 5x5 units long, using $D = 0.06$ and $E = 0.1$ for diffusion. Fitness graphs for some typical runs are shown in figure 5 a). As it can be seen from the graph, evolution tends to occur with sudden jumps in fitness, but this can be justified by the fitness function alone, and it should not be related to the model itself. The currently used fitness function does not allow for a wide range of different values, therefore dynamics of this kind will always occur whenever this fitness function is used.

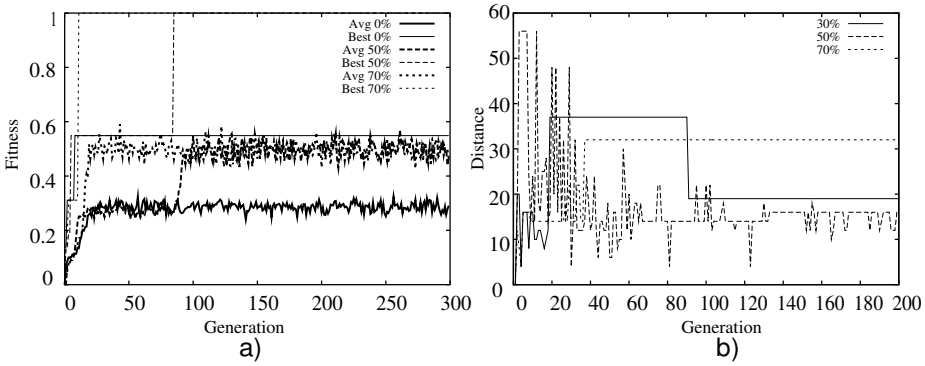

Fig. 5. a) Fitness graph b) Offspring sensitivity to maternal effects (both for the placental model with $mD = 0.2$).

For further establishing the influence of maternal effects, we devised a simple distance measure between the neural networks. As the number and type of neurons are fixed for all the neural networks, we defined the distance between two networks as the total number of links that are unshared between them. Using this distance measure, we picked up the best individuals on each generation, grow them again without any maternal influence ($mt = 0$), and computed the distance between them. By doing this, we could therefore estimate the degree of sensitivity to maternal effects in each offspring. Typical results for a run are shown in figure 5 b). As it can be seen, offspring sensitivity tends to oscillate widely in the first generations, until eventually becoming stable. These oscillations, however, are only following dynamics in individual diversity, and on themselves do not show sensitivity to be adaptive. That is, diversity in offspring sensitivity in the earlier generations is only reflecting the larger diversity in the individuals in the initial population pool; as evolution progresses, the population diversity decreases, and therefore offspring sensitivity to maternal effects becomes stable.

For investigating any further influence in adaptiveness, we computed the average fitness over all generations, in all runs sharing the same mt parameter, with the results depicted in figure 6 a). Although this process may hide any special dynamics that may happen during evolution, at least it is able to show if there is any strong influence from the increasing mt values. All the three sets exhibit different effects on adaptiveness, with the two different models showing, in fact, opposite effects: the cytoplasmic model has an overall negative adaptive effect, while the placental model shows a positive one. For the $mD = 0.2$ experiments, maternal influence above 70% shows a roughly 30% increase in average fitness, a significant improvement ($p = 0.03$ with ANOVA). For $mD = 0.8$, however, this influence becomes stale, probably due to the mD value being too high.

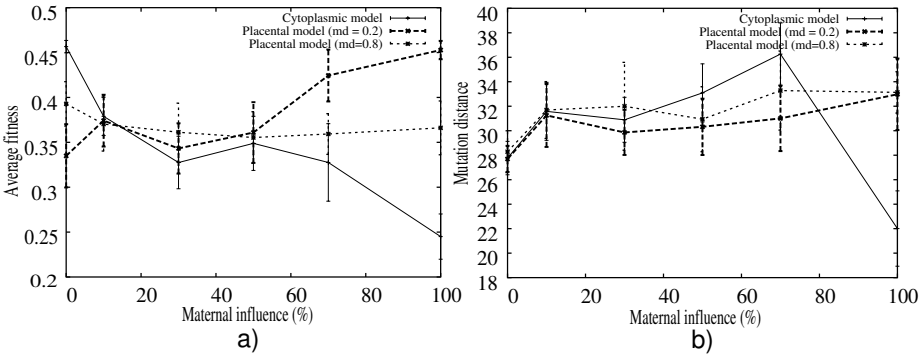

Fig. 6. a) Average fitness value for the runs, classified by increasing maternal influence. b) Robustness to mutations with increasing maternal influence. (average value + standard error)

In our opinion, there are three possible reasons for this improvement. Maternal influence may be positively affecting: 1) sensitivity to mutations, 2) development, or 3) selection response. For checking the first hypothesis, we performed mutation experiments in the best individuals, and computed the average distance created by mutations. We picked up all the best individuals in all generations, mutated them once (generating children), and computed the distance between the original individual and its child. The procedure for mutation, and for computing the distance between the networks were the same as explained before. This process was repeated 10 times for each individual, and grouped by maternal influence. This, however, is not a good metric for computing mutation sensitivity, because development in the best individuals still has a strong influence from their own mothers. Therefore, we also performed mutation experiments where the individual was mutated twice in a serial fashion, yielding a grandchild; the distance computed was then between the original individual and its grandchild. Both experiments turned out to yield similar results, and the results for this latter case can be seen in figure 6 b). Maternal influence increased slightly the

mutation sensitivity (except for the extreme case of 100%, in the cytoplasmic model), but this does not seems to be related to the adaptiveness increase. As for the second hypothesis, the placental model may be positively affecting development, by increasing diversity in the connections between neurons. In our model, redundant connections are ignored in the networks, and therefore increasing the number of connections can be a suitable strategy employed by evolution. Because the mother and offspring genotypes are different, they express different kinds of substances, that could increase link diversity in the offspring as the substances are exchanged. If the exchange rate is too high, however, it may prove too disruptive and therefore the effect is lost. We are currently checking this hypothesis, and also if delay in selection response occurs.

4 Conclusion

We presented two different models, reflecting two different mechanisms for maternal effects, using simulated development and a genetic algorithm. In our experiments, the cytoplasmic model exhibited decreased adaptiveness in finding solutions, while the placental model showed significant adaptive improvements, especially with higher values of maternal influence, and with low exchange rates between mothers and offspring. This positive effect, however, was shown not to be related to any effect in mutation sensitivity. We are currently checking other possibilities for this effect, namely if maternal effects are influencing link diversity in the networks, or if they are delaying response to selection.

References

1. David E. Cowley. Genetic prenatal maternal effects on organ size in mice and their potential contribution to evolution. *Journal of Evolutionary Biology*, 4(3), May 1991.
2. Peter Eggenberger, Gabriel Gomez, and Rolf Pfeifer. Evolving the morphology of a neural network for controlling a foveating retina - and its test on a real robot. In Russell K. Standish, Mark A. Bedau, and Hussein A. Abbass, editors, *Proceedings of the Eighth International Conference on Artificial Life*, pages 243–251. MIT Press, 2002.
3. D. S. Falconer. Maternal effects and selection response. In S. J. Geerts, editor, *Genetics today, Proceedings of the XI international congress on genetics*, pages 763–774. Pergamon Press, Oxford, 1965.
4. Frederic Gruau. *Neural Network Synthesis using Cellular Encoding and the Genetic Algorithm.* PhD thesis, Laboratoire de la Informatique du Parallelisme, Ecole Normale Superieure de Lyon, 1994.
5. Mark Kirkpatrick and Russell Lande. The evolution of maternal characters. *Evolution*, 43(3):485–503, May 1989.
6. MaryCarol Rossiter. Incidence and consequences of inherited environmental effects. *Annual Review of Ecology and Systematics*, 27:451–476, November 1996.
7. Jason B. Wolf, Edmund D. Brodie III, James M. Cheverud, Allen J. Moore, and Michael J. Wade. Evolutionary consequences of indirect genetic effects. *Trends in Ecology and Evolution*, 13(2):64–69, February 1998.