A model for phenotype change in a stochastic framework

Fields 2008

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Outline

- 1. Introduction to the biology
- 2. Nishimura's deterministic model
- 3. A stochastic model of Plasticity
- 4 Results
- 5. Discussion of the stochastic model
- 6. Generalisations: Developmental time

Under Development: deterministic

1. Introduction

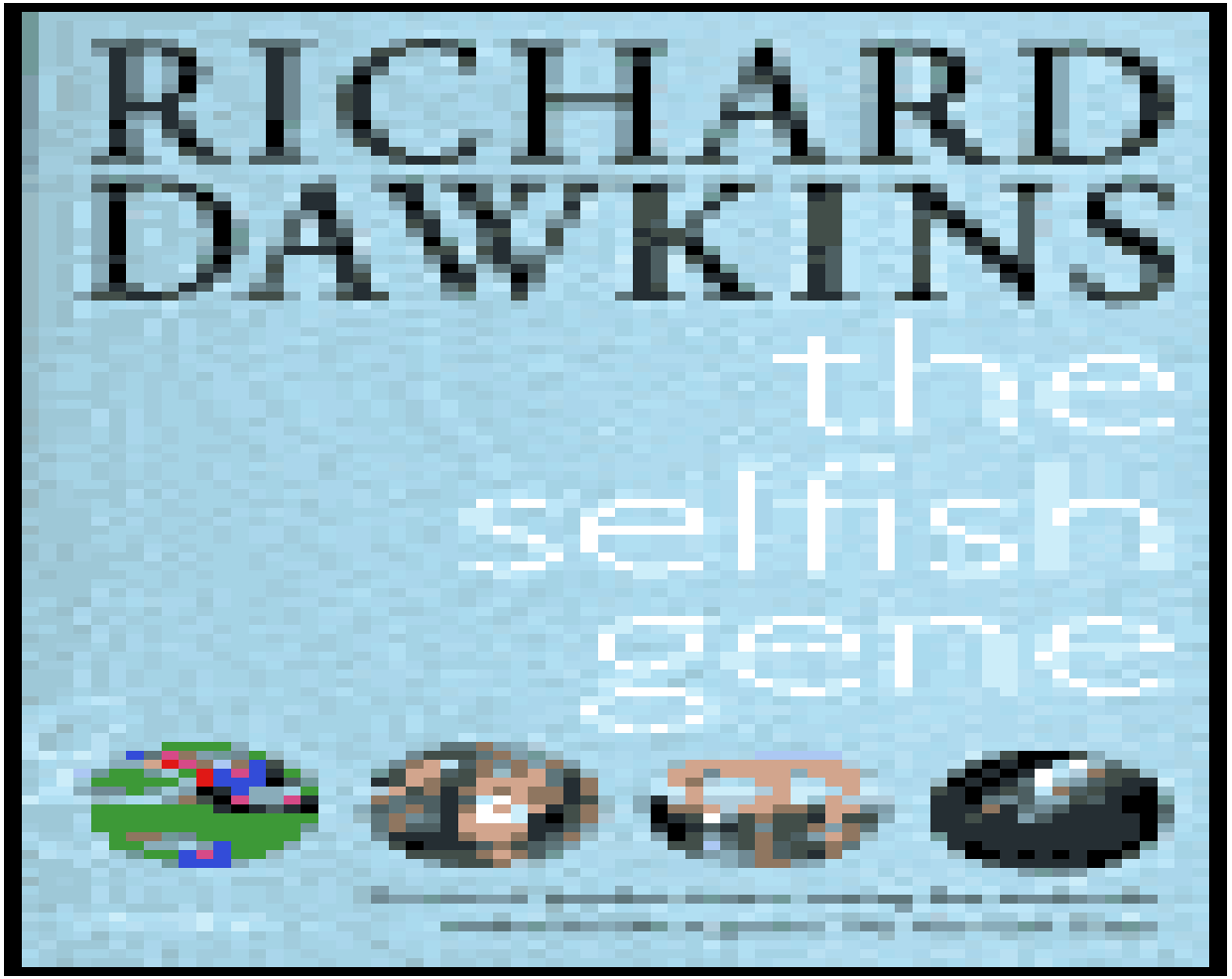
- An organism may express different phenotypes (gene expression) in response to changes in the environment. This phenomenon is called plasticity and appears to be an important mechanism enhancing an organism's ability to survive and reproduce.
- That is, plasticity induces a fitness advantage for the organism.

- Nishimura (2006)* proposed that an organism faced with a change in environmental circumstances would seek to minimise the energy cost of adapting to the new environment and the energy cost of reproduction. To illustrate these concepts Nishimura (2006) constructed a simple model of a “prey” in an environment which changes to favour “predation”. The prey may elicit a plastic response to reduce predation, but this response will require extra energy to induce.

* ***Nishimura,K. “Inducible plasticity; optimal waiting time for the development of an inducible phenotype”, Evolutional Ecology Research, Vol 8, 2006, pp 553-559.***

- If the predation rate increases it destroys the population fitness;
- Changes in the characteristics are initiated with consequential changes in the Energy content.

Popularized in….



- In epidemiology, a popular theory is that the rising incidences of coronary heart disease and Type II diabetes in human populations undergoing industrialization is due to a mismatch between a metabolic phenotype determined in development and the nutritional environment during development, to which an individual is subsequently exposed. This is known as the

  'Thrifty phenotype' hypothesis.

2. Nishimura's deterministic model

- Assume a prior specific death rate of μ_1 for the "prey" and, when the environment changes, it has a death rate of μ_2 (with $\mu_1 > \mu_2$) and that the development of the plastic response incurs an energy cost from a base of c_0 to c_1 (with $c_0 < c_1$).

- **A fitness function *W(t)* for the suitable fitness currency as a function of time *t* at which the plasticity is expressed - linking the predation rate to the energy cost of the plastic response:**

$$W(t) = e^{-(\mu_1 t + \mu_2 (T-t))}[E - c_0 t - c_1 (T-t)] \qquad (1)$$

The first term = the survival probability in the predator environment;
The second term = the amount of remaining energy;
where T = total time, t = the switching time,
E = total energy budget, W = "plasticity",
c_i = the Energy consumption rate in the respective modes i= 0,1.

c_o is the default baseline energy cost to the prey individual per time, and

c_1 includes the additional costs of building and maintaining the defensive phenotype per unit time, $c_1 > c_o$.

$$W(t) = e^{-(\mu_1 t + \mu_2 (T-t))}[E - c_0 t - c_1 (T-t)]$$

This is a simple counting exercise.

- Now differentiate w.r.t *t* …….

- Nishimura uses equation (1) to find the maximum fitness response for the time at which plasticity is expressed following the change in the environmental conditions which most advantages predation. This is found to be trivially, $W`(t) = 0$, at which time the plasticity is (actually) maximised, which gives:

$$t^* = \frac{1}{\mu_1 - \mu_2} \frac{E - c_1 T}{c_1 - c_0} \qquad (2)$$

- But this assumes a deterministic approach in cohort where there is no variability,

So……. Introduce variability…

3. **A Stochastic Model of Plasticity**

- Suppose that the fitness of the organism at time *t* given by equation (1) is now a stochastic variable. In terms of pressure for the development of plasticity it is the expected value of the fitness that is of interest. That is, the time of plastic response *t* that maximises the expected value of the fitness is of interest in determining the evolutionary path.

- Let $\alpha = \mu_1 - \mu_2 > 0$
- $A = E - c_1 T$
- $c = c_1 - c_o > 0$

Then

$$W(t) = e^{-\alpha t - \mu_2 T}[A + ct] \qquad (2)$$

Let the time of the plastic response be a normally distributed random variable with mean $\bar{t}$ and variance σ_t^2. Note this is not assuming *W* is Gaussian, only its components.

Q. Should this be a Beta distribution????

- Then the expected value of the fitness of the organism is:

$$E[w(t)] = E[e^{-\alpha t-\mu_2 T}[A+ct]]$$

$$= e^{-\mu_2 T} E[e^{-\alpha t}(A+ct)]$$

$$= e^{-\mu_2 T} AE[e^{-\alpha t}] + ce^{-\mu_2 T} E[te^{-\alpha t}]$$

Noting that

$$E[te^{-\alpha t}] = e^{-\alpha\bar{t}+\frac{1}{2}\alpha^2\sigma_t^2}(\bar{t}-2\alpha\sigma_t^2)$$

Then we get

$$E[w(t)] = e^{\frac{1}{2}\alpha^2\sigma_t^2 - \alpha\bar{t} - \mu_2 T}\left(A + c(\bar{t} - 2\alpha\sigma_t^2\right) \quad (3)$$

- Note that equation (3) is similar to the deterministic case expressed by equation (1) with $t \rightarrow \bar{t} - \alpha\,\sigma_t^2$:

$$W(t) = e^{-(\mu_1 t + \mu_2 (T-t))}[E - c_0 t - c_1 (T-t)]$$

- Equation (3) has 2 variables associated with the plasticity, the time of the response in relation to the environmental stimulus and the variance of this response in the population of interest . Finding the maximum fitness by differentiating with respect to each of these variables and setting to zero gives the two inconsistent equations:

$$\alpha c\left(\bar{t} - \alpha\sigma_t^2\right) = c - \alpha A$$
$$\alpha c\left(\bar{t} - \alpha\sigma_t^2\right) = 2c - \alpha A \qquad (4)$$

- The fitness of the organism is maximised when plasticity acts at the time from the environmental stimulus given by:

$$\bar{t}^{*} = \frac{1}{\alpha} - \frac{A}{c} + \alpha\sigma_t^2 \qquad \bar{t}$$

$$= \frac{1}{\mu_1 - \mu_2} - \frac{E - c_2 T}{c_2 - c_1} + (\mu_1 - \mu_2)\sigma_t^2 \quad (5)$$

This uses the first equation $\partial/\partial\bar{t} = 0$.

- This shows that when the time of plasticity is stochastic then the mean time of plasticity optimising the expected value of the fitness is extended by an amount given by $\alpha\sigma_t^2$. In this respect variation in the response of plasticity in the population might be seen as an advantage in terms of providing extra time for the average response in the population to be most effective.

- However, in terms of Life History analysis the variance of the response to plasticity might be regarded as the variable of interest. That is, an organism might seek to optimise fitness by manipulating the variance of the response, perhaps by collecting a variety of alleles or by developing epigenetic modes to express such variation. In this case the optimum variance of plasticity to maximise the fitness is given by:

$$\hat{\sigma}_t^2 = \frac{1}{\alpha}\left(\bar{t} - \frac{1}{\alpha} + \frac{A}{c}\right)$$

$$= \frac{1}{\mu_1 - \mu_2}\left(\bar{t} - \frac{1}{\mu_1 - \mu_2} + \frac{E - c_2 T}{c_2 - c_1}\right)$$

-

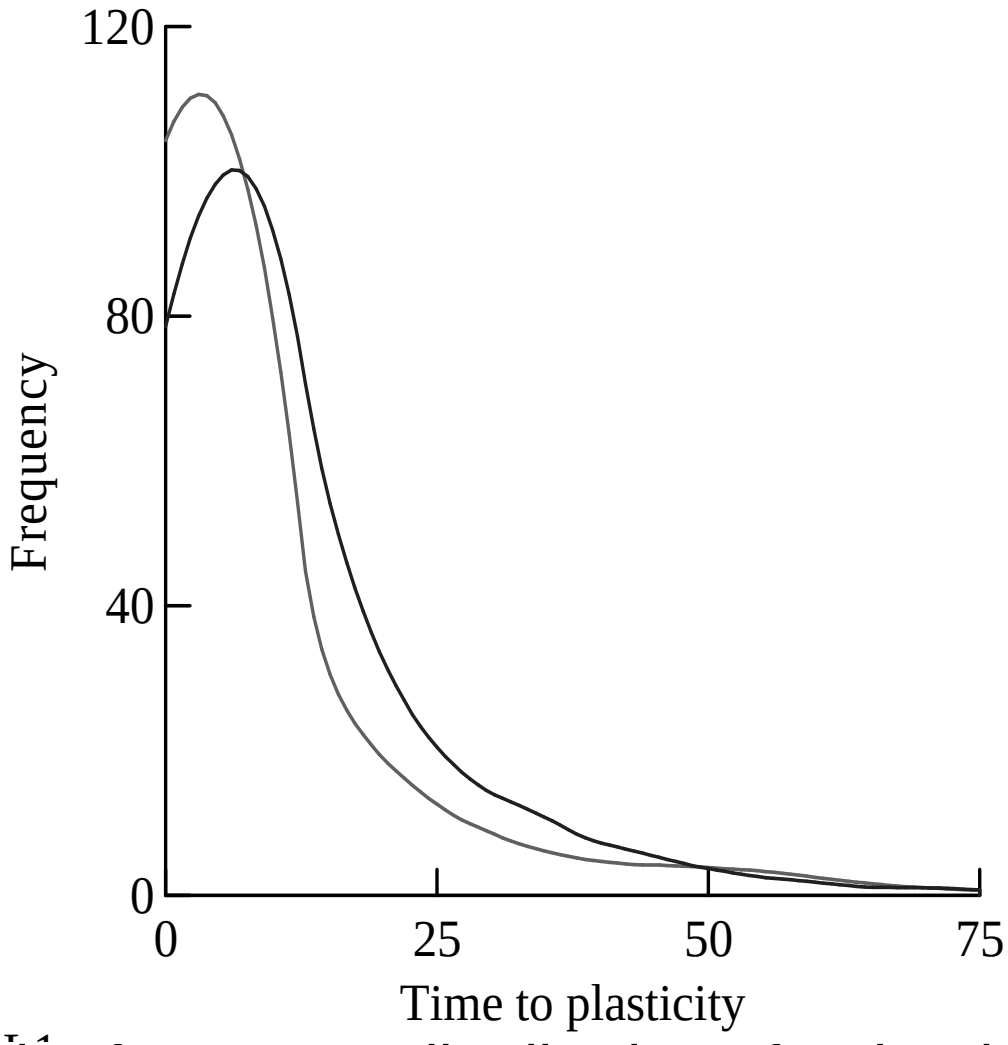
4. Results

- However, the results show that the maximum expected value of fitness is not given by an unique pair of numbers for the average time of plasticity and the variance of plasticity, but rather by a set of numbers lying on a straight line in the plane of the average time and the variance of plasticity. Repeating this here…..*New term*

$$\bar{t}^{*} = \frac{1}{\alpha} - \frac{A}{c} + \alpha\sigma_t^2$$

$$= \frac{1}{\mu_1 - \mu_2} - \frac{E - c_2 T}{c_2 - c_1} + (\mu_1 - \mu_2)\sigma_t^2$$

- This is shown on the following diagram:



- **Figure 2:** The frequency distributions for the time to plasticity for 2 populations each having the same optimal expected value for fitness given by equation (3).

- A population might not be on the optimal mean time – variance of plasticity line for a number of reasons. For example, the average energy available *E* might change, resulting in a parallel shift of the optimum mean time variance line, or the predation rates might change altering the slope.

- If the population ends up off the optimal line the question arises of the expected path in the mean time of plasticity – variance of plasticity space that it will take to get to the new optimal line.

- To calculate this path we assume that the probability distribution of time *t* to switch states (the plasticity factor for the population) remains Gaussian. This means that the new environment induces a similar average change in *t* across the population, preserving the Gaussian character of its probability density.

Transition to a new optimal state:

- Assuming that the path of the population in mean time of plasticity – variance of plasticity space proceeds in a direction most favourable to the population this means

  that the path from a point $(\bar{t}_0, \sigma^2_{0,t})$

  to a point $(\bar{t}_1, \sigma^2_{1,t})$ on the new optimal line .

  That is, the population will follow a path that is perpendicular to the level curves of the expected value of the fitness function (3).

- Let x = variance,

  y = mean time

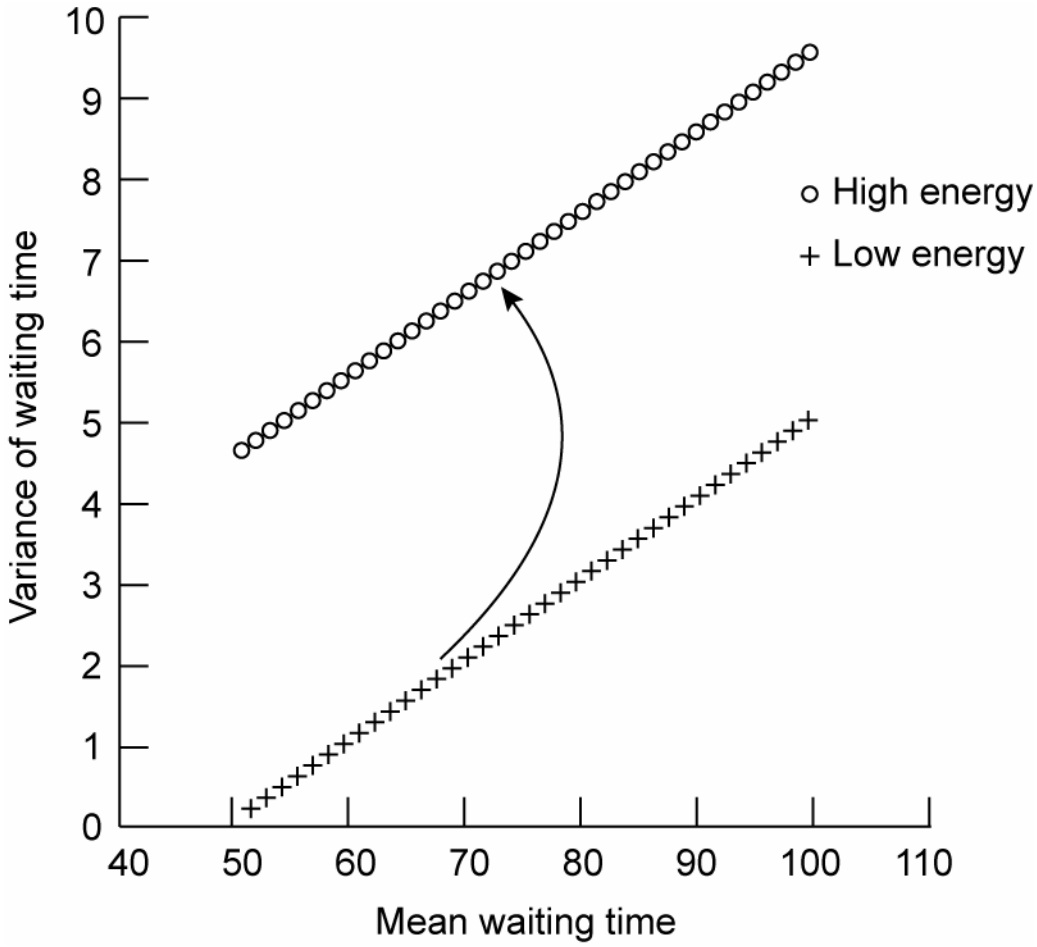
  w_1 = maximum of the expected value of fitness, with available energy is E_1; $w_1 = F(x,y)$

Then $E_1 \rightarrow E_2$

The path to w_2 = maximum of the expected value of fitness, with available energy E_2 will follow the o.d.e

$$\frac{dy}{dx} = \frac{\partial F/\partial y}{\partial F/\partial x}$$

which is perpendicular to the level curves, that is the steepest path. This is shown in the following diagram…it is obtainable analytically!!!!



- **Figure 3.** The trade – off between the expected value of the time for plasticity and the variance of the time for plasticity in a population subjected to 2 different energy availabilities, and the optimal path of time to plasticity mean and variance when the energy available changes from low to high.

Consider a population with

T = 100 days,

an average energy level of 100 units,

$\mu 1 = 0.2$, $\mu 2 = 0.1$ days^{-1}

$c1 = 0.5$, $c2 = 2$ units. days^{-1}

standard deviation $\sigma = 8$ days.

This will have an optimal average time to optimal plasticity of 84.1 days. (The deterministic calculation is 77.7 days, that is, 6.4 days less).

If the energy level available from the environment changes to 105 units then the equations imply the population will move to an optimal mean time for plasticity of 81.8 days with a standard deviation of 7.2 days.

Example continued

The extra energy available results in a shorter time to implement plasticity, because the population has more energy to spare on maintaining plasticity for a longer time.

Energy	Mean time	Std Deviation
100	84.1 days	8 days
105	81.8 days	7.2 days

Outcomes in Red

4. Discussion

- The analysis presented here shows a relationship between the average time for plasticity and the variance of the time for plasticity.
- The higher the variance the longer the average time for plasticity that maximises the organism's fitness.
- If there was a constraint which acted to ensure that plasticity required some minimum time, the organism might adjust the variance of the time for plasticity to maximise fitness.

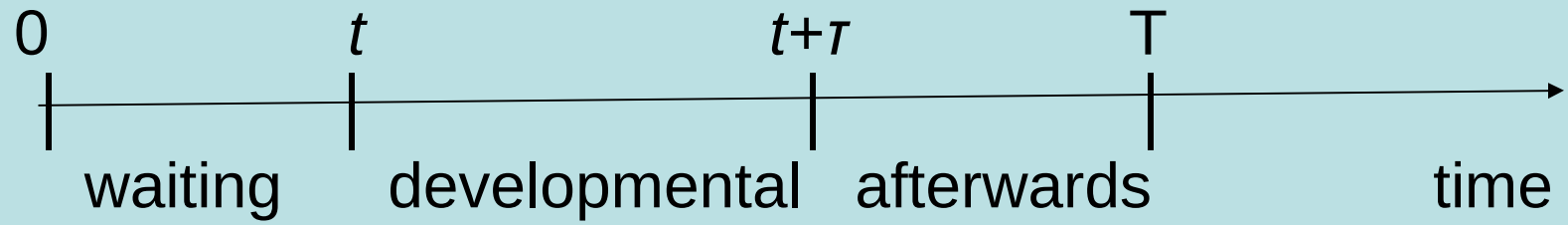
- The smaller the difference between the death rates the greater the variance which ensures maximum fitness (for a given average time for plasticity).
- Alternatively, the greater the difference between death rates the smaller the variance for maximum fitness.
- Similarly for the energy cost of implementing plasticity.
- The moments (1st and 2^{nd}) of the optimal distribution are obtained by a shift in available energy easily by solving a first order o.d.e.

6. Deterministic Generalisation

- After an environmental cue is detected, the organism waits for a period t before initiating development of the induced phenotype, which takes time τ. During this waiting time the constant per unit-time cost of the yet to be induced phenotype is c_1, and the death rate μ_1 is also constant. During development, these parameters change to c_d and μ_d, respectively, and after development is complete they become c_2 and μ_2. Although we do not assume so, biological considerations imply that

$$c_d > c_2 > c_1.$$

Similarly, it seems reasonable to infer that $\mu_1 > \mu_d, > \mu_2$.



- We investigate various different realistic forms of c_d :

  (a) first, that the product $c_d\tau$ is a constant, D, which can be thought of as the (fixed) cost of development;

  (b) second, that c_d is a constant, and so the cost of development is a linearly increasing function of development time, τ, that is,

$$D(\tau) = c_d \tau$$

and, finally,

(c) we put $D(\tau) = K_0 + K_d e^{-r\tau}$

where K_o, K_d and r are constants, which implies that rapid development is more expensive: the cost of development, , is now a decreasing function of the development time. Fitness is evaluated at a time T, measured from the onset of the environmental cue.

- Again following, Nishimura (2006), we assume that the total initial energy budget is a constant, E, and the background cost of plasticity reduces this energy by a constant amount c_0. If the environment does not change (and there is no cue), therefore, the total cost to the organism is $c_0 + c_1 T$. If the organism detects the cue and develops the induced phenotype, the cost is

$$c_0 + c_1\left(t+\tau\right) + c_2\left(T-t-\tau\right)$$

- . The proportion of the population which survives is, following Nishimura (2006),

$$\exp[-\left(\mu_1 t + \mu_d \tau + \mu_2\left(T-t-\tau\right)\right)]$$

- and hence the fitness function is

$$W(t,\tau) = e^{-\mu_1 t} e^{-\mu_d \tau} e^{-\mu_2 (T-t-\tau)} \left[E - c_0 - c_1 t - c_d \tau - c_2 (T-t-\tau) \right]$$

- Nishimura's (2006) Equation (1) can be recovered by substituting $c_d = c_1$ and $\mu_d = \mu_1$.
- This formulation assumes the cue is always detected and is perfectly reliable. It is important to realize that the evolution of plasticity may be favored even when these two assumptions are violated (Moran 1992; Sultan & Spencer 2002).

References

- Moran, N.A. 1992. The evolutionary maintenance of alternative phenotypes. American Naturalist 139: 971-989.
- Sultan, S.E. and H.G. Spencer. 2002. Meta-population structure favors plasticity over local adaptation. American Naturalist 160:271-283.
- Wake, G.C., A.B. Pleasants, A. Beadle and P.D. Gluckman. 2008. The optimal waiting time for the induction of plasticity for a phenotype in a population subject to random environmental effects. (to appear).

Procedure for these modifications

- Proceed as before, optimise the fitness function on the region

$$\{(t, \tau) : 0 < t + \tau < T\}.$$

Note: The maximum may, for some parameter values not be an internal maximum.

This is trivial calculus really with big impact.

Summary

- Phenotypic plasticity is ubiquitous in the biological realm and it has fundamental consequences for our understanding of evolution.
- The realization that the induced response need not begin immediately after the environmental cue has generally been under-appreciated by evolutionary biologists.

- Such a delay may have important consequences for fitness and, indeed, some recent authors have argued that a number of phenotypic changes observed in adult humans and other mammals that have deleterious health effects (e.g., diabetes, hypertension), are in response to inappropriate environmental cues detected as a fetus or newborn .

- It is further claimed that the physiological mechanisms underlying many of these delayed responses have been selected and we label them

  “predictive adaptive responses.”

PAR is an in-topic right now amongst evolutionists.

- Here we have extended Nishimura's model in four ways:

(1) we introduce a cohort and focus on the probability distribution of development time;

(2) we allow the parameters during development to be different, albeit constant, from those during the waiting time which we introduced;

(3) we permit development time to be a variable and optimize it *simultaneously* with waiting time;

(4) we assume that the cost of developing the induced phenotype is an exponential function of development time (details omitted).

This has enormous effect on phenotype plasticity and organism development especially for a fetus.

Any Questions??

FETAL DEVELOPMENT

From zygote to full term.

For McGraw-Hill Publishing

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