Reprinted from
GENES IN ECOLOGY

The 33rd Symposium of
The British Ecological Society
University of East Anglia

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Blackwell Scientific Publications
Oxford London Edinburgh Boston
Melbourne Paris Berlin Vienna
1991
INTRODUCTION

No organism can do everything. Every creature is restricted by constraints of various kinds. Many of these arise from the facts of history and the nature of evolution, both of which can proceed only from where they left off. This systems view of constraint — that living things have so many functional interconnections that it becomes difficult for evolution to reverse itself — is implicit in much of the literature. Natural selection has, it is supposed, produced the best available balance between components of life history such as age at maturation and number of offspring.

Physical and chemical laws also impose mechanical limits on how an animal, a cell or a genome operates. Molecular biology sees the structure of genes as being as much a chemical consequence of the nature of the genetic material as an evolved trade-off among its functions. Both views of constraint are needed to understand how any living system operates but neither is in itself enough to explain its limitations.

Here we illustrate the dual nature of constraint on patterns of reproduction and survival in relation to size, the causes of being small and fast as opposed to large and slow. Limits to growth and reproduction arise both from evolutionary history and from the mechanics of replication, from Darwin’s organ-grinder and Mendel’s monkey. The balance between them has some surprising effects on life history. Nearly all living systems — genes, cells and organisms — grow discontinuously as one generation succeeds another. This leads to a mechanical constraint as dividing systems have a size threshold below which the next stage of development cannot be initiated. There may also be natural selection on growth through variations in size at the beginning of each growth cycle, and through
variation in growth rates. This produces a trade-off between size, age at maturation and rate of multiplication. Reproductive constraints on size may be similar at the organismal, the cellular and the DNA level. Research on tractable systems showing mechanical constraint may give an insight into the behaviour of systems less open to experiment.

**Daphnia Moulting: A Mechanical Constraint on Life History**

The life history of *Daphnia* (Fig. 16.1) has several elements: discontinuous growth (an unavoidable consequence of a rigid exoskeleton); genetic or environmental variation in size at birth; a threshold size for initiation of maturation and ovarian development; and variation in growth rates. Consider a series of freshly hatched first instar *Daphnia*, each slightly larger than the last (Fig. 16.1). The first just crosses the size threshold in its third moult. After two more molts it matures, having had five juvenile instars. The next four, each slightly larger at birth, also cross the threshold in their third moult. They define an instar group, within which all individuals have had five instars. Within this instar group and when growth rates are constant, the pattern is simple; size at maturity increases with size at birth. In contrast, the size at birth of the sixth individual in Fig. 16.1 is so

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**Fig. 16.1.** The threshold model. Simulated growth steps for 10 female *Daphnia* from the first instar to the instar of first reproduction. Each step represents one instar, and the next instar length is 30% greater than the one preceding it. In the instar reached after passing the threshold egg production is initiated and takes two instars. The five animals smallest at birth (solid lines) took six instars to reach the reproductive stage, while the five larger newborns (dashed lines) took five instars to do so.
great that the threshold is crossed in the second moult and it matures after four molts. This means that the sixth individual is larger at birth than the fifth but smaller at maturity. Discontinuous growth coupled with a size threshold can reverse the ranks of sizes at birth and sizes at maturity but only does so between instar groups, not within them (Ebert 1991).

This can have unexpected effects on life history. Figure 16.2a shows the relation between size at birth and size at maturity for two groups of

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**Fig. 16.2.** Transformation of a distribution of size at birth into a distribution of size at maturity. (a) Relationship between length at birth and length at maturity. Newborns too small to reach the threshold size in the same instar as their larger sibs grow through one instar more and become larger at maturity. (b) A distribution of sizes at birth is transformed into a distribution of sizes at maturity.
Daphnia females with different numbers of instars at maturity. Figure 16.2b shows a typical unimodal distribution of sizes at birth. Individuals in the right-hand portion of the distribution are large enough at birth to cross the threshold in their second moult and mature in the fifth instar. Within this instar group, size at maturity increases with size at birth in a straightforward fashion. Those in the left-hand portion of the distribution are smaller at birth, require one more instar to mature, and are larger at maturity than those in the other instar group. They form a second mode in the distribution, which is unimodal at birth but bimodal at maturity. There may hence be very different distributions for size at maturity from particular ranges of size at birth.

This can have important selective effects. For example, there is selection for large size at birth under conditions of limited food (Tessier et al. 1983). Mean size at maturity would then decrease rather than increase. How selection on size at maturity might be transformed into selection on size at birth depends on several factors (Fig. 16.3). Figure 16.3a shows the relationship of size at birth to size at maturity for two instar groups (6 instars and 5 instars). The points are laboratory data from D. magna, and the lines are the best fit to these points. They represent the situation depicted schematically in Fig. 16.2a. Figure 16.3b shows five hypothetical ranges of size at birth, with the hatched portions indicating individuals that are killed and the white portions those selected. The influence on size at birth of selection for large or small adult size is not simple.

In distribution 1, all individuals are large enough at birth to need only five juvenile instars. If there is directional selection on size at maturity so that all individuals larger than 3.3 mm at maturity are killed, there is also directional selection for the individuals that were smaller at birth. Distribution 2, however, has a range that overlaps the five and six instar groups. Individuals requiring five instars to mature are smaller than those needing six instars to do so, so that directional selection downwards on size at maturity is transformed into directional selection upwards on size at birth. Distribution 4 is just as broad as distribution 3 but is shifted with respect to the threshold sizes at birth that separate the instar classes. It results in a transfer of directional selection on size at maturity into disruptive selection on size at birth. Distribution 5, broadest of all, results in a transformation of size at maturity into a more complex kind of disruptive selection. It emphasizes the unexpected consequences of small changes in the initial conditions of growth.

This has implications for phenotypic covariance. Within an instar group, for a fixed growth rate, size at maturity increases with size at birth. Under the same conditions age at maturity also increases with size at birth (Ebert 1991) and the phenotypic correlation between age and size at
maturity is positive. If size at birth is fixed and growth rates vary (for example, because of variation in juvenile food supply), then the correlation becomes negative. In nature there will be diversity in size at birth and in juvenile growth rate. Depending on which combination applies the phenotypic correlation of age and size at maturity could vary from strongly positive to strongly negative. A small change in the initial conditions of size and growth rate can have large effects on the phenotypes of the adult population, and hence on subsequent generations. In particular, it may alter their demography because of the effects of adult size on fecundity, leading, for example, to a loss of synchrony and the rapid appearance of a wide range of age and size classes.
In *Daphnia* an ancient constraint on growth, the exoskeleton, combined with a size threshold for maturation leads to complex and surprising relationships between size, selection and phenotypic covariances. The *Daphnia* size-dependent maturation threshold ensures, at the cost of additional instars, that individuals do not mature at too small a size. There is variation in instar numbers in spiders (Deevey 1949), decapods (Hartnoll 1985), Lepidoptera (Clare & Singh 1991) and locusts (Uvarov 1966) and other groups. However, in Diptera, Hymenoptera and Coleoptera the number of pre-adult instars is fixed. If this were true in *Daphnia*, adults would be small when growth is poor (as in fruitflies and bumblebees; Plowright & Jay 1968, Gebhardt & Stearns 1988). If, as in *Daphnia*, juvenile growth is about equal in each juvenile instar, a fixed number of instars leads to a positive correlation between size at birth (or egg size) and size at maturity. It also predicts age at maturity, which is then likely to be a continuous rather than a discontinuous function of growth, as is the case when instar number varies (see Fig. 16.1). This may help to ensure synchrony of mating partners, or the ratio of adults to juveniles in social organisms. When a fixed number of juvenile instars leads to costs in terms of small adult size these may be convertible into a cost in age at maturity. The tobacco horn worm *Manduca sexta* always pupates in the fifth instar. If growth is poor, maturation can be delayed until this instar reaches a critical weight (Nijhout & Williams 1974).

MECHANICAL CONSTRAINTS AND CELL DIVISION

This mechanism of growth, with its need to attain a threshold before reproduction, has consequences for the ecology, demography and evolution of *Daphnia*. It amplifies small differences in growth rate to produce large differences in life history. There may be analogies here with the life histories of cells and genes. The rate of cell division is itself subject to mechanical constraint. For example, rapidly growing *E. coli* cells can divide every 20 minutes or so, twice as fast as the maximum rate of DNA replication. The cost of replicating the DNA is deferred by initiating a subsequent cycle of DNA replication before the end of the preceding cell division. Individual *E. coli* cells may contain one, two, three or more replication forks; and as cell size depends on DNA content they differ in size at cellular maturity (Lewin 1990). This mechanism means that any slight genetic or environmental difference in growth rate early in the history of an *E. coli* population is rapidly amplified as particular cells attain (or fail to attain) the critical ratio between DNA content and cell mass needed for the subsequent division; a pattern comparable to that in
Daphnia and one which may have similar demographic effects on subsequent generations. In particular it may lead to the rapid loss of synchrony in cell cultures.

In eukaryotes, too, a cell must attain a critical point in the cell cycle before it is primed for division (Alberts et al. 1989). There is a series of controls which trigger the onset of mitosis in developing tissues (O'Farrell et al. 1989). Any slight variation, genetic or environmental, which affects the time when it reaches the trigger point and the decision whether to divide or to continue to grow can have large effects on later cell generations. In cells — as in Daphnia — limitation of growth leads to an arrest at some point in the division cycle (Pardee 1989). Any such mechanism which involves discontinuous growth and a size threshold will ensure that a newly founded population — of bacteria, yeast or Daphnia — rapidly develops a wide range of age and size classes, thus reducing intraspecific competition. It will also affect patterns of tissue differentiation in multicellular organisms.

Tissue growth is limited by the need to replicate DNA and assemble each new cell. The strength of this constraint is manifest in the early embryo (Alberts et al. 1989, Hartwell & Weinert 1989). DNA replication takes place very rapidly after fertilization but this can be achieved only by the mother's provisioning the unfertilized egg with the precursors needed for cell division. Although the cells divide rapidly, they do not grow: thousands of cells may arise by cleavage of the egg within a few hours with no increase in overall mass as succeeding cells become smaller and smaller. Once the developing embryo begins to grow the rate of cell division decreases greatly; there is a trade-off between size at cellular maturity and rate of growth. The existence of cell cycle mutations which change the relationship between cell size and cell maturity (Murray & Kirschner 1989) may provide an experimental system for exploring the effects of growth thresholds on the life histories of cells.

**DNA REPLICATION AS A MECHANICAL CONSTRAINT**

DNA replication is a physically and chemically complicated business which takes time and energy, so that the rate of reproduction can be constrained by the nature of the genetic material. The E. coli genome has about two million base pairs (bp). At optimal temperatures replication proceeds at about 50,000 bp per minute, so that it cannot take less than 40 minutes to produce the new copy of the DNA required by a daughter cell (Lewin 1990, Watson et al. 1987). Any increase in genome size has a
physical cost in terms of reproductive rate. The insertion of a plasmid slows the replication process (Zund & Lebek 1980).

E. coli, unlike most eukaryotes, has little repetitive DNA or untranscribed sequences within functional genes. The traditional view that bacteria are primitive has been abandoned: modern bacteria are a diverse and highly adapted group. Their lack of introns and repeated sequences may be a size trade-off arising from the strong selection for life history components, in particular for rapid reproduction in creatures who repeatedly show exponential growth in numbers. The need to copy the functional minimum of DNA may hence limit the age at which reproduction takes place. Any excess genetic material slows this process and selection has eliminated it. The same process may explain why most eukaryotic mitochondria are free of intervening sequences. Mitochondria can divide rapidly. They compete for membership in the fraction passed on at cell division. All their genes are functional, and indeed some seem to have been shipped off to the nucleus during their evolution. To be speedy, the mitochondrial genome is forced to be small; and how quickly it can replicate is constrained by how small it can get.

The same life history trade-offs apply in viruses, whose economical genome is the epitome of the sacrifice of size for speed of reproduction. Viral genes may even overlap, with the same DNA sequence coding for different products when read from different starting points (Lewin 1990). ‘Incomplete’ viruses of plants have a shorter genome than do their complete relatives and reproduce at their expense by taking advantage of some of their DNA sequence. This provides an escape from the constraints imposed by the mechanics of replication but imposes an evolved constraint of its own, a dependence on the presence of complete viruses. Mobile DNA elements have to face the same mechanical compromises. In Drosophila, shorter transposable elements (such as P elements) multiply more frequently than do longer ones (Charlesworth & Langley 1989). ‘Incomplete’ P elements have deleted part of their sequence. They increase their reproductive rate by taking advantage of the replication machinery of complete elements to escape from the mechanical constraint on speed and size at maturity. Their number is limited by the number of complete elements available; and the number of complete elements is itself restricted by their cost to the host.

**DISCUSSION**

The $10^8$ range in body size in the living world is accompanied by a $10^6$ difference in the length of DNA. In many creatures, the vast majority of
the genome seems to be without function and must exert a cost in replication. There are some correlations between the amount of DNA and life history parameters at both cellular and organismal levels, suggesting that the mechanics of replication may act as a constraint (Cavalier-Smith 1985). In protozoa, genome size is negatively correlated with intrinsic rate of natural increase (Shuter et al. 1983). Eukaryotic cells with excess chromosomes (such as B chromosomes and perhaps trisomic cells in humans) appear to divide more slowly. Cancer cells treated with methotrexate may produce multiple copies of detoxifying genes; and this slows their division. Metastasizing cells in a tissue may have aberrant amounts of DNA when compared to normal cells (Weatherall 1991). They frequently lose any of the synchrony present in the parental tissue (Pardee 1989), perhaps because of the effects of DNA content on changing growth rate and, as in *Daphnia*, amplifying small initial differences in rate of growth because of the presence of a threshold size for division.

At the organismal level, too, the amount of DNA is correlated with life history parameters such as age at maturation. In copepods, species with larger genomes grow more slowly (McLaren et al. 1989). In Amphibia, developmental time may increase with DNA content. This is well seen in plethodontid salamanders, in which those with high C-value have a torpid life-style, with a low rate of limb differentiation and long lives (Sessions & Larson 1987). Although there is no general fit between DNA content and life history parameters in plants, those species whose growth involves increase in cell size rather than in cell number do have larger genomes (Grime et al. 1985). Other associations between genome size and life history are reviewed by Cavalier-Smith (1985). Although genome size tends to be correlated with slow growth or cell division, this is not always so: in cyprinid fishes, for example, in which there is variation in DNA content among individuals and among species there is no apparent fit of genome size with variation in life history (Gold et al. 1990).

Of course, not all cases of delayed maturity are related to such mechanical constraints. Maturity may be delayed for adaptive reasons of life history: a delay increases size and hence fecundity, or improves physiological condition so that offspring mortality is reduced to an extent which compensates for a longer juvenile period (Stearns & Crandall 1981). However, there are real mechanical constraints on age at maturity: these range from the basic need to carry out a set number of DNA replications and cell divisions to the equivalent need to pass through a series of instars before maturity. There is enough phenotypic plasticity in rate of growth and age at maturity to ensure that when growth rates are reduced and maturity delayed there may — as in *Daphnia* — be either
larger or smaller size at maturity, and hence changes in the demography of the populations of cells or organisms being studied. However, the commonest pattern is that reduced growth rates result in delayed maturity at a smaller size (Stearns & Koella 1986).

Why, then, are some genomes congested with DNA that has no apparent function and seems to slow replication? It is possible that such DNA has some as yet unknown role but most favour the idea that such sequences are 'selfish': that they multiply without reference to the effects on the fitness of their carriers. For example, the numbers of copies of mobile elements such as Drosophila P elements is limited by their deleterious effects on their carriers (Charlesworth & Langley 1989). Although the target of selection is not known, reduced growth rate imposed by the need to replicate excess DNA may be a good candidate.

It may be that delayed maturity usually evolves for some adaptive reasons, and that only then can excess DNA accumulate. Studies of cell size (a good measure of DNA content) in some fossils do suggest that species early in an evolving lineage have relatively small genomes, and that large quantities of DNA accumulate in derived taxa (Conway Morris & Harper 1988). In a slowly growing species, selection pressures to keep the cell cycle short and the genome small are considerably reduced. This could allow DNA content to increase to an extent determined by the delay in maturity. It may then be difficult to get rid of this excess DNA should demographic pressures be reversed. In creatures with short life cycles, selection is stronger on age at maturity than it is on other fitness components (such as fecundity). However, in those with long slow life cycles selection on fecundity becomes much more important than that on age at maturity (Stearns 1992). Only in species that already mate at a relatively early age is selection likely to be able to lead to the ejection of excess DNA and to even earlier maturity. A slow life cycle may be an evolutionary impasse whose limits are defined by the invasion of redundant DNA.

These speculations — and they are little more than that — about the interaction between life-history theory and molecular biology suggest some avenues which might be explored. Do taxa which appear to have gained large amounts of repeated sequence DNA recently have a later age at maturity than their relatives? Are evolutionary reversals of size and life history accompanied by decrease in DNA content? This seems to be true for bacteria and mitochondria but is it the case for, say, dwarf mammals on islands and hymenopteran parasitoids of insect eggs which have been selected for small size and speedy lives? An apparent contradiction to this view is that the tiny plethodontid salamander Thorius
(which matures relatively young) has a very large genome but in this species cells divide slowly but differentiate rather rapidly (Roth et al. 1988). Might there be differences in DNA content or cell size among Drosophila lines selected for high or low rates of maturation; or an association between the response to selection for early maturation and DNA content? It may be possible to use lines differing in DNA content to test whether redundant DNA does have a direct effect on body size and on age at maturity.

Whatever the merit of these ideas it is clear that demographic adjustments of the timing of age at maturity operate under constraints set by the mechanics of molecular biology and cell division as much as by the machinations of natural selection.

REFERENCES


