RESEARCH COMMENTARY

Genetic correlations: transient truths of adaptive evolution

N. G. PRASAD[1] and MALLIKARJUN N. SHAKARAD[2]

[1]*Department of Biology, Queen's University, Kingston, Ontario K7L 3N6, Canada*
[2]*Behaviour, Ecology and Evolution Laboratory, Biology Department, Poornaprajna Institute of Scientific Research, 4, Sadashivanagar, Bangalore 560 080, India*

Satyaanubhava-vellaringa-mondentahudu?
Bettadadiyolagobba kodabaliyobba
Ettarada drushya kaniveyolihanigaadeete
Netradandade nota, Manku thimma

(D. V. Gundappa, Kannada poet)

(How can the experience of Truth be the same for all?
One is at the bottom of the hill and the other at the top
Can the view from the top be for the one in the valley?
Your view is as good as your sight, Manku thimma.)

(Translation by authors)

The concept of 'truth', arguably, exists only in the discourse of poets and mathematicians. The rest of us have to make do by replacing the sublime 'truth' by the more mundane 'consistency'. Much thinking in evolution is based on the implicit notion of consistency in the relationship among fitness traits, relationships that can either facilitate or constrain certain evolutionary trajectories being taken by a population. Such thinking is exemplified by the notion of trade-offs that is ubiquitous in the study of life-history evolution (Prasad and Joshi 2003). Formal theory, on the other hand, clearly suggests that genetic correlations can change in the process of adaptive evolution, being partly a function of allele frequencies (Falconer 1981). Thus, the question remains as to whether, genetic correlations among traits are really consistent across populations and evolutionary time, at least in the short to medium term? Though several studies have previously addressed the issue of consistency of trait correlations within and across environments (e.g. Wilkinson *et al*. 1990; Joshi and Thompson 1995, 1997; Bell 1997), three recently published studies (Archer *et al*. 2003; Chippindale *et al*. 2003 and Phelan *et al*. 2003) deserve mention for their magnitude and scope, experimental design and rigour, and the consequent ability to determine the causes for change in trait correlation with greater confidence by controlling for various confounding factors. All three studies from the same laboratory, were done on populations of *Drosophila melanogaster* descended from a common ancestral population, and under similar maintenance and assay conditions. These studies show that (a) trait correlations can change over few tens of generations even in a controlled laboratory environment, (b) selection – rather than linkage disequilibrium, inbreeding or genotype × environment (G × E) interaction – is the major factor that changes trait correlations, at least in these studies, and (c) long-term laboratory selection experiments, though technically and logistically daunting, offer breath-taking insights into the subtleties of the process of adaptive evolution, which would be difficult by following other experimental approaches.

The relevance and importance of these studies to experimental evolution in particular, and evolutionary thought in general, becomes clear if we consider the process of adaptive evolution. The evolutionary trajectory of a population depends, to a large extent, on the interplay between selective forces acting on the population and the genetic architecture of fitness components, where the genetic architecture can be defined as the pattern of genetic correlations among traits relevant to fitness. The evolutionary trajectories are further affected by chance. Therefore, it follows that, given the long time scale and, hence, the number of contingent events expected to occur, it is highly improbable that one can predict macro-evolutionary trends with

E-mail: prasad@biology.queensu.ca; mallik99@jncasr.ac.in.

Keywords. genetic architecture; life history; experimental evolution; genetic correlations; genotype × environment interaction; stress resistance; *Drosophila melanogaster*.

a high degree of confidence. Further, the very existence of a diversity of life-histories argues in favour of changing trait correlations, at least over large macro-evolutionary time scales. Thus, our ability to predict evolutionary trajectories of populations is probably limited to micro-evolutionary time scales, and this too under the assumption that trait correlations are stable, at least on such small time scales. So we return to the basic question being addressed by the three studies (Archer *et al*. 2003, Chippindale *et al*. 2003 and Phelan *et al*. 2003): can one define a stable genetic architecture, at least on a time scale on the order of a few tens of generations? We concentrate on the studies by Archer *et al*. (2003) and Phelan *et al*. (2003), because both these studies investigate the same trait correlation, that between stress resistance and longevity, but much of what we have to say is also true for the study of Chippindale *et al*. (2003), which documents the breakdown of a correlation between pre-adult growth rate and pre-adult survivorship under intense selection for rapid pre-adult development.

Phelan *et al.* (2003) analyse the correlation between stress (starvation and desiccation) resistance and longevity, using a comparative approach involving assaying these traits on 75 different laboratory populations representing 15 different selection regimes, each replicated five-fold. The selection regimes studied include selection primarily for early life fertility, late life fertility and longevity, rapid development, starvation resistance under a variety of nutritional regimes, and desiccation resistance. At the time of this study, most populations had experienced their respective selection regimes for more than 35 generations. Though many previous studies using both phenotypic manipulations (Chippindale *et al*. 1993) and laboratory selection (Service *et al*. 1985, Rose *et al*. 1992) have shown a positive correlation between stress resistance and longevity, Phelan *et al*. (2003) show that this correlation breaks down at very high levels of stress resistance, indicating a complex, non-linear relationship between stress resistance and longevity. At low to moderate levels of stress resistance, longevity and stress resistance appear to be positively correlated, in that populations exhibiting relatively higher stress resistance also show relatively higher longevity. Under direct selection for stress resistance, moderate increases in stress resistance lead to concomitant increases in longevity. Similarly, in populations selected for increased or decreased longevity, there is a parallel change in stress resistance. However, at high levels of stress resistance, this correlation breaks down and even appears to be negative with the populations selected to have the highest stress resistance showing fairly low longevity.

In principle, changes in trait correlations observed in a laboratory setting may be due to G × E interactions. To examine this possibility, Phelan *et al*. (2003) assayed longevity in three different environments on a subset of the 75 populations. Although they observed a significant effect of assay environment on longevity, there was no evidence for a G × E interaction on longevity. Thus, differences in the longevities of stress selected populations were most likely not an artifact of G × E interaction induced by the assay environment. Changes in trait correlation can also result from linkage disequilibrium, inbreeding depression, or selection. However, the study of Phelan *et al*. (2003) – being essentially a comparative study in which among-population comparisons are confounded with selection, both past and present – can provide only a weak resolution among these possible factors causing changes in trait correlations. The complementary study of Archer *et al*. (2003) tracks within-population trait correlations during the course of selection for starvation or desiccation resistance, and thus provides a much clearer resolution of the potential factors affecting trait correlations during laboratory selection.

Archer *et al* (2003) selected populations of *D. melanogaster* for increased stress (starvation and desiccation) resistance and looked at correlated changes in longevity over many generations. Selection for increased stress resistance resulted in a parallel increase in longevity over the first 10–20 generations, indicating a positive genetic correlation between the two stress resistance traits and longevity. However, continued selection for increased desiccation resistance eventually led to a reduction in longevity, which returned to more or less control levels after ~160 generations of selection; clear evidence that the initial positive correlation between the two traits had changed into a negative correlation in the course of selection. Similarly, continued selection for increased starvation resistance resulted in a decline in longevity between generations 20 and 75, and thereafter longevity appeared to be relatively unchanged over a further 30–35 generations, at a level about 25% of what it had been at generation 20, although still higher than the longevity of control populations. The results of these two studies provide a clear indication that trait correlations are unstable, and can change in sign over even few tens of generations.

The degree of population replication and large effective population sizes used in these two studies, along with the large number of loci affecting the phenotype for composite traits like stress resistance and longevity, make it unlikely that either linkage disequilibrium or inbreeding are the cause of the reversal in sign of the changing trait correlations. Hence, we are left with the possibility that selection itself is the main factor altering trait correlations, at least in these populations. There are three ways in which selection could alter the genetic correlation between traits, and these are not mutually exclusive:

(a) Selection for stress resistance may also be imposing concomitant selection for longevity, without the two traits being genetically correlated. As a result, longevity could increase in the initial generations of selection. Possibly, the subsidiary selection for longevity ceases after some

generations, while selection for stress resistance continues. This mechanism, however, cannot explain a decrease in longevity in the later generations of selection, while stress resistance continues to increase.

(b) Longevity in stress selected populations evolves as a secondary effect with increases in the initial phase of selection and decreases in the later phase of selection. The initial increases in longevity may simply be due to increased resource storage, reflecting positive pleiotropy between stress resistance and longevity. However, at very high levels of stress resistance, the high levels of stored resources may extract a cost in terms of decreased longevity. Here, it is the nature of pleiotropy for stress resistance and longevity that is postulated to change, due to the altered physiological background in highly stress resistant flies.

(c) There may be differential recruitment of alleles. Alleles that simultaneously enhance longevity and stress resistance will be favoured initially and will go to fixation. The remaining alleles that increase stress resistance may be ones that are either neutral or detrimental with respect to longevity. Similar arguments have been made for the evolution of tradeoffs between components of performance in different environments (Joshi and Thompson 1995), and there is some empirical support for these arguments from studies on both laboratory (Joshi and Thompson 1997) and field (Ballabeni and Rahier 2000; Ueno *et al*. 2003) populations.

The studies of Archer *et al*. (2003) and Phelan *et al*. (2003) describe a change in the correlation between stress resistance and longevity from positive early in the course of strong directional selection for stress resistance to negative later on. Chippindale *et al*. (2003), in a comparative study similar in conception to that of Phelan *et al*. (2003), and utilizing a set of 55 populations partly overlapping with those used by Phelan *et al*. (2003), show that a tradeoff between pre-adult survivorship and pre-adult growth rate (higher growth rate is accompanied by reduced survivorship) is seen only in populations not directly selected for pre-adult fitness traits. In populations subjected to directional selection for rapid development, both pre-adult survivorship and pre-adult growth rate decline as correlated responses to selection. Results from a previous study selecting for rapid pre-adult development (Prasad *et al*. 2000) show that the decline in pre-adult growth rate is apparent over the full first 70 generations of selection, whereas the decline in survivorship does not become apparent till about 50 generations of selection have elapsed. Taken together, it is clear from the results of these studies that genetic correlations among traits can vary across populations, and within populations over generations, suggesting that the genetic architecture of fitness can rapidly evolve under the influence of selection. So where does this leave our notion of a 'genetic architecture'? Chippindale *et al*. (2003) suggest that the idea of 'a tractable genetic architecture underlying life-history is a sanguine intellectual mistake', and we agree. The results discussed here highlight the dynamic nature of the genetic architecture of fitness related traits. In principle, one can get to know the genetic architecture of a population at equilibrium in great detail. But these details do not take one far in predicting the evolutionary trajectory once the population is no longer at genetic equilibrium. This almost transient nature of trait correlations underscores the subtlety of the process of adaptive evolution.

Sandehavee-krutiyol-inilla-vendalla
Indu nambihude mundendu-mendalla
Kundu-tordand-adanu tiddikole manasuntu
Indigee matavuchita, Manku thimma

(D. V. Gundappa, Kannada poet)

(It is not that this work is free of doubts
What's true today may not be tomorrow
With an open mind to correct mistakes when they show up
This position is good for today, Manku thimma.)

(Translation by authors)

References

Archer M. A., Phelan J. P., Beckman K. A. and Rose M. R. 2003 Breakdown in correlations during laboratory evolution. II. Selection on stress resistance in *Drosophila* populations. *Evolution* **57**, 536–543.

Ballabeni P. and Rahier M. 2000 A quantitative genetic analysis of leaf beetle larval performance on two natural hosts: including a mixed diet. *J. Evol. Biol.* **13**, 98–106.

Bell G. 1997 *Selection: the mechanism of evolution*. Chapman and Hall, New York.

Chippindale A. K., Leroi A. M., Kim S. B. and Rose M. R. 1993 Phenotypic plasticity and selection in *Drosophila* life-history evolution. I. Nutrition and the cost of reproduction. *J. Evol. Biol.* **6**, 171–193.

Chippindale A. K., Ngo A. L. and Rose M. R. 2003 The devil in the details of life-history evolution: instability and reversal of genetic correlations during selection on *Drosophila* development. *J. Genet.* **82**, 133–145.

Falconer D. S. 1981 *Introduction to quantitative genetics*, 2nd ed. Longman, London.

Joshi A. and Thompson J. N. 1995 Trade-offs and the evolution of host specialization. *Evol. Ecol.* **9**, 82–92.

Joshi A. and Thompson J. N. 1997 Adaptation and specialization in a two-resource environment in *Drosophila* species. *Evolution* **51**, 846–855.

Phelan J. P., Archer M. A., Beckman K. A., Chippindale A. K., Nusbaum T. J. and Rose M. R. 2003 Breakdown in correlations during laboratory evolution. I. Comparative analyses of *Drosophila* populations. *Evolution* **57**, 527–535.

Prasad N. G. and Joshi A. 2003 What have two decades of laboratory life-history evolution studies on *Drosophila melanogaster* taught us? *J. Genet.* **82**, 45–76.

Prasad N. G., Shakarad M., Gohil V. M., Sheeba V., Rajamani M. and Joshi A. 2000 Evolution of reduced pre-adult viability and larval growth rate in laboratory populations of *Drosophila melanogaster* selected for shorter development time. *Genet. Res.* **76**, 249–259.

Rose M. R., Vu L. N., Park S. U. and Graves J. L. 1992 Selection on stress resistance increases longevity in *Drosophila melanogaster*. *Exp. Gerontol*. **27**, 241–250.

Service P. M., Hutchinson E. W., MacKinley M. D. and Rose M. R. 1985 Resistance to environmental stress in *Drosophila melanogaster* selected for postponed senescence. *Physiol. Zool*. **58**, 380–389.

Ueno H., Fujiyama N., Yao I., Sato Y. and Katakura H. 2003 Genetic architecture for normal and novel host-plant use in two local populations of the herbivorous ladybird beetle, *Epilachna pustulosa*. *J. Evol. Biol*. **16**, 883–895.

Wilkinson G. S., Fowler K. and Partridge L. 1990 Resistance of genetic correlation structure to directional selection in *Drosophila melanogaster*. *Evolution* **44**, 1990–2003.