3. Boucher, Y., Douady, C.J., Papke, R.T., Walsh, D.A., Boudreau, M.E.R., Nesbø, C.L., Case, R.J., and Doolittle, W.F. (2003). Lateral gene transfer and the origins of prokaryotic groups. Annu. Rev. Genet. *37*, 283–328.
4. Richards, T.A., Dacks, J.B., Jenkinson, J.M., Thornton, C.R., and Talbot, N.J. (2006). Evolution of filamentous plant pathogens: gene exchange across eukaryotic kingdoms. Curr. Biol. *16*, 1857–1864.
5. Simpson, A.G.B., and Roger, A.J. (2004). The real 'kingdoms' of eukaryotes. Curr. Biol. *14*, R693–R696.
6. Latijnhouwers, M., de Wit, P.J., and Govers, F. (2003). Oomycetes and fungi: similar weaponry to attack plants. Trends Microbiol. *11*, 462–469.
7. Dean, R.A., Talbot, N.J., Ebbole, D.J., Farman, M.L., Mitchell, T.K., Orbach, M.J., Thon, M., Kulkarni, R., Xu, J.R., Pan, H., *et al*. (2005). The genome sequence of the rice blast fungus *Magnaporthe grisea*. Nature *434*, 980–986.
8. Genereux, D.P., and Logsdon, J.M., Jr. (2003). Much ado about bacteria-to-vertebrate lateral gene transfer. Trends Genet. *19*, 191–195.
9. Loftus, B., Anderson, I., Davies, R., Alsmark, U.C.M., Samuelson, J., Amedeo, P., Roncaglia, P., Berriman, M., Hirt, R.P., Mann, B.J., *et al*. (2005). The genome of the protist parasite *Entamoeba histolytica*. Nature *433*, 865–868.
10. Andersson, J.O. (2005). Lateral gene transfer in eukaryotes. Cell. Mol. Life Sci. *62*, 1182–1197.
11. Huang, J., Mullapudi, N., Lancto, C.A., Scott, M., Abrahamsen, M.S., and Kissinger, J.C. (2004). Phylogenomic evidence supports past endosymbiosis, intracellular and horizontal gene transfer in *Cryptosporidium parvum*. Genome Biol. *5*, R88.
12. Ricard, G., McEwan, N.R., Dutilh, B.E., Jouany, J.P., Macheboeuf, D., Mitsumori, M., McIntosh, F.M., Michalowski, T., Nagamine, T., Nelson, N., *et al*. (2006). Horizontal gene transfer from bacteria to rumen ciliates indicates adaptation to their anaerobic carbohydrates rich environment. BMC Genomics *7*, 22.
13. Andersson, J.O., Hirt, R.P., Foster, P.G., and Roger, A.J. (2006). Evolution of four gene families with patchy phylogenetic distribution: influx of genes into protist genomes. BMC Evol. Biol. *6*, 27.
14. Bhattacharya, D., Yoon, H.S., and Hackett, J.D. (2004). Photosynthetic eukaryotes unite: endosymbiosis connects the dots. Bioessays *26*, 50–60.
15. Archibald, J.M., Rogers, M.B., Toop, M., Ishida, K., and Keeling, P.J. (2003). Lateral gene transfer and the evolution of plastid-targeted proteins in the secondary plastid-containing alga *Bigelowiella natans*. Proc. Natl. Acad. Sci. USA *100*, 7678–7683.
16. Keeling, P.J., and Inagaki, Y. (2004). A class of eukaryotic GTPase with a punctate distribution suggesting multiple functional replacements of translation elongation factor 1α. Proc. Natl. Acad. Sci. USA *101*, 15380–15385.
17. Koski, L.B., and Golding, G.B. (2001). The closest BLAST hit is often not the nearest neighbor. J. Mol. Evol. *52*, 540–542.
18. Wenzl, P., Wong, L., Kwang-Won, K., and Jefferson, R.A. (2005). A functional screen identifies lateral transfer of β-glucuronidase (gus) from bacteria to fungi. Mol. Biol. Evol. *22*, 308–316.
19. Doolittle, W.F. (1998). You are what you eat: a gene transfer ratchet could account for bacterial genes in eukaryotic nuclear genomes. Trends Genet. *14*, 307–311.
20. Takishita, K., Ishida, K., and Maruyama, T. (2003). An enigmatic GAPDH gene in the symbiotic dinoflagellate genus *Symbiodinium* and its related species (the order Suessiales): possible lateral gene transfer between two eukaryotic algae, dinoflagellate and euglenophyte. Protist *154*, 443–454.

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DOI: 10.1016/j.cub.2006.08.042

Frequency-Dependent Selection: When Being Different Makes You Not Stand out

A recent study reports frequency-dependent survival within highly variable guppy populations. Fitness advantages to rare genotypes may help maintain variation within populations, but the mechanisms underlying these advantages require further study.

Patrik Nosil

Biologists have long been fascinated with systems exhibiting extremely high levels of phenotypic or genotypic variation, such as immune system genes, host–pathogen systems [1] and color polymorphisms [2,3]. This fascination stems from a classic evolutionary paradox: directional and stabilizing selection are common [4] and should decrease variation and thus preclude high diversity within populations [5,6]. But there is another form of selection that can maintain variation — frequency-dependent selection favoring rare variants [7]. In their recent experimental field study, Olendorf *et al.* [8] have demonstrated frequency-dependent survival within guppy populations, with rarer male phenotypes showing enhanced survival. These new findings provide novel insights into the maintenance of extreme variation in male color within a classic research system, Trinidadian guppies, and suggest that frequency-dependent selection might play a role in solving the paradox of high within-population variation.

Under frequency-dependent selection, the fitness of an individual depends on the relative frequency of its phenotype. The concept dates back to Darwin [9], who wrote that "the most distinct varieties … have the best chance of succeeding", and it was expanded over the next century into theories for the maintenance of genetic variation [7]. In particular, the idea emerged that visual predation can generate frequency-dependent selection, such that prey risk increases with the relative frequency of the prey type [2,3,10]. Such a process may occur, for example, if predators form a search image for common prey thereby decreasing the risk of rare prey [11]. During such frequency-dependent predation, being rare does not necessarily equate to standing out in the crowd.

Guppies are a model system in ecology and evolutionary biology, and they exhibit particularly variable male color-patterns [12–14]. These color-patterns are subject to opposing patterns of directional natural and sexual selection; bright males exhibit mating advantages but are subject to greater predation risk [12–14]. Although there is previous evidence for a rare-male mating advantage [14], the possibility of a rare-male survival advantage remained untested until a recent study by Olendorf *et al.* [8]. The authors manipulated the frequency of guppy morphs in replicate streams, such that one morph was rare in some replicates (at a ratio of 1:3) but common in

other replicates (3:1). The survival of these marked guppies was then tracked using mark-release-recapture techniques. In multiple streams and years, the rarer phenotype had a strong survival advantage because of frequency dependent selection. Importantly, this rare phenotype advantage was independent of the actual 'color morph' of the male (Figure 1A). Thus extreme variability in male color-pattern may be maintained by trade-offs between directional natural and sexual selection, combined with rare-male mating and survival advantages (Figure 1B).

As in most other systems, the precise mechanism that gives a survival advantage to rare guppy males remains unknown. Olendorf *et al.* [8] suggest two possibilities. First, predators (larger fish) may form a search image for common prey. And second, male guppies may alter their behavior in response to changes in relative morph frequency, with differential survival being related in some way to these altered behaviors. Although predation was the apparent source of mortality, its presence was not manipulated, so other factors cannot be ruled out. Future work should focus on elucidating the factors that generate frequency-dependent selection within populations, not only for cases of predation, but also for intraspecific competition (for example [15]).

Frequency-dependent selection has been studied extensively in a different yet conceptually related context: divergence between populations. Again, it was Darwin [9] who noted that frequency-dependent selection can drive population divergence and speciation: "the principle of benefit derived from divergence of character … will generally lead to the most divergent variations … being preserved and accumulated by natural selection … until a sufficient amount of variation has been accumulated to form it into a well-marked variety…". One idea is that similar phenotypes compete disproportionately for food resources, generating frequency-dependent selection that can split a phenotype

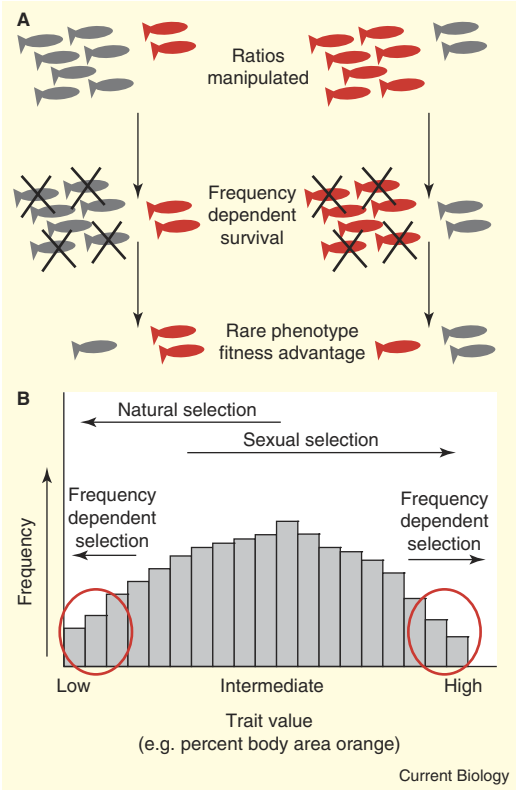

Figure 1. Frequency-dependent selection within guppy populations.

(A) Rare phenotypes have a survival advantage, independent of color 'morph'. (B) Contrasting patterns of directional natural and sexual selection, coupled with frequency-dependent selection, maintain variation within guppy populations. Natural selection favors duller, more cryptic males. Sexual selection favors brighter, more conspicuous males. Frequency-dependent selection favors whichever phenotypes are rare.

distribution in two [16,17]. This process underlies many theoretical models of adaptive radiation [17] and speciation [18], and has been detected in recent empirical studies of adaptive radiation [17]. A recent paper [19] reported evidence for incipient speciation in a particularly divergent and strikingly colorful form of guppy, raising the question of whether frequency dependence played a role in its evolution.

The parallels and contrasts between studies of extreme variation within *versus* between populations should yield powerful insights into the maintenance and generation of biodiversity, from immune systems, to guppies, rain forests, and coral reefs. Both within and between populations, frequency-dependent selection can critically affect the evolution of variation and divergence. Thus far, most researchers studying within-population variation have, like Olendorf *et al.* [8], focused mainly on survival and predation [20]. In strong contrast, studies of between-population divergence have emphasized resource competition. Future studies examining the exact mechanisms underlying frequency-dependent selection should help determine whether different selective processes underlie the maintenance of variation within populations versus divergence between populations. Ultimately, we would like to know how the two levels of variation are connected — can frequency-dependent selection provide a bridge between microevolution within populations and divergence among species? If so, a unified theory for the role of frequency-dependent selection in the origin and maintenance of diversity may emerge.

References

1. Borhgans, J.A.M., Beltman, J.B., and De Boer, R.J. (2004). MHC polymorphism under host-pathogen coevolution. Immunogenetics *55*, 732–739.
2. Endler, J.A. (1988). Frequency-dependent predation, crypsis, and aposematic coloration. Phil. Trans. R. Soc. Lond. B *319*, 505–523.
3. Clark, B. (1962). Balanced polymorphism and the diversity of sympatric species. In Taxonomy and Geography, D. Nichols, ed. (Oxford: Systematics Association), pp. 47–70.
4. Kingsolver, J.G., Hoekstra, H.E., Hoekstra, J.M., Berrigan, D., Vignieri, S.N., Hill, C.E., Hoang, A., Gibert, P., and Beerli, P. (2001). The strength of phenotypic selection in natural populations. Am. Nat. *157*, 245–261.

5. Fisher, R.A. (1930). The Genetical Theory of Natural Selection (Oxford: Claredon press).
6. Lewontin, R.C. (1964). The interaction of selection and linkage. II. Optimum models. Genetics *50*, 757–782.
7. Ayala, F.J., and Campbell, C.A. (1974). Frequency-dependent selection. Annu. Rev. Ecol. Syst. *5*, 115–138.
8. Olendorf, R., Rodd, H.F., Punzalan, D., Houde, A.E., Hurt, C., Reznick, D.N., and Hughes, K. (2006). Frequency dependent survival in natural guppy populations. Nature *441*, 633–636.
9. Darwin, C. (1859). On the Origin of Species by Means of Natural Selection or the Preservation of Favoured Races in the Struggle for Life. Reprinted 1964 (Cambridge, MA: Harvard University Press).
10. Allen, J.A. (1988). Frequency-dependent selection by predators. Philos. Trans. R. Soc. Lond. B *319*, 485–503.
11. Tinbergen, L. (1960). The natural control of insects on pinewoods. I. Factors influencing the intensity of predation by songbirds. Arch. Neerlandaises. Zool. *13*, 265–343.
12. Endler, J.A. (1980). Natural selection on color pattern in Poecilia reticulata. Evolution *34*, 76–91.
13. Endler, J.A., and Houde, A. (1995). Geographic variation in female preferences for male traits in Poecilia reticulata. Evolution *49*, 456–468.
14. Brooks, R. (2002). Variation in mate choice within guppy populations: population divergence, multiple ornaments, and maintenance of polymorphism. Genetica *116*, 343–358.
15. Bolnick, D.I. (2003). Can intraspecific competition drive disruptive selection? An experimental test in natural populations of sticklebacks. Evolution *58*, 608–618.
16. Slatkin, M. (1979). Frequency- and density-dependent selection on a quantitative character. Genetics *93*, 755–771.
17. Schluter, D. (2000). The Ecology of Adaptive Radiation (Oxford: Oxford University Press).
18. Alexander, H.J., and Breden, F. (2004). Sexual isolation and extreme morphological divergence in the Cumaná guppy: a possible case of incipient speciation. J. Evol. Biol. *17*, 1238–1254.
19. Dieckmann, U., Doebeli, M., Metz, J.A.J., and Tautz, D. (2004). Adaptive Speciation (Cambridge: Cambridge University Press).
20. Merilaita, S. (2006). Frequency-dependent predation and the maintenance of prey polymorphism. J. Evol. Biol. *46*, 1–9.

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DOI: 10.1016/j.cub.2006.08.038

Centrosome Duplication: Is Asymmetry the Clue?

The structure of the yeast Sfi1–centrin complex, and its asymmetric position within the yeast centrosome, suggest a model for the initiation of centrosome duplication and provides a target for licensing this event.

Michele H. Jones and Mark Winey

Centrosomes, the yeast equivalents of which are known as spindle pole bodies (SPBs), are microtubule-organizing centers of eukaryotic cells, which are made up of proteins but, like chromosomal DNA, are replicated in a tightly regulated manner that is coordinated closely with the cell division cycle. The mechanism of centrosome duplication is poorly understood, but insights are coming from studies of components such as centrin, a small calcium-binding protein that was first identified in the flagella of green algae [1]. Centrins have turned out to be ubiquitous, widely conserved proteins, now known from a variety of studies to be involved in assembly, and in some cases maintenance, of centrosomes, SPBs and the basal bodies of flagellae [2,3]. The involvement of centrin in multiple cellular processes, some calcium-dependent and some not, suggested that alternative binding partners would be discovered for the protein that define particular functions, and this has turned out to be the case. Several years ago, Kilmartin [4] uncovered a novel yeast protein called Sfi1 which binds centrin in the absence of calcium, is conserved in vertebrates and localizes to centrosomes in both yeast and vertebrates. Now, Kilmartin and colleagues [5] have reported a structural analysis of the Sfi1–centrin complex and its asymmetric arrangement in the SPB (Figure 1), the results of which suggest a plausible model for the initiation, if not the licensing, of SPB duplication.

Sfi1 contains approximately 20 repeats that are similar to a subset of IQ domains initially identified in unconventional myosins [6], where they were shown to mediate binding to calmodulin, another small, calcium-binding protein. Structures have been determined for two different co-crystals of Sfi1 repeats with bound centrin: one with two repeats crystallized in low calcium, and one with three repeats that required calcium to make suitable crystals [5]. Interestingly the structure is not significantly altered by calcium, suggesting little role for calcium binding by centrin in its interaction with Sfi1. The centrins on adjacent Sfi1 repeats interact in a head-to-tail manner, and some mutations that affect the interacting parts of centrin were found to disrupt function *in vivo* [5,7]. The Sfi1 repeats themselves are extended α helices, leading to the idea that Sfi1 is an elongated protein stabilized by centrin binding at one molecule per repeat. Li *et al.* [5] provided support for this stoichiometry by showing that a shortened Sfi1 containing only

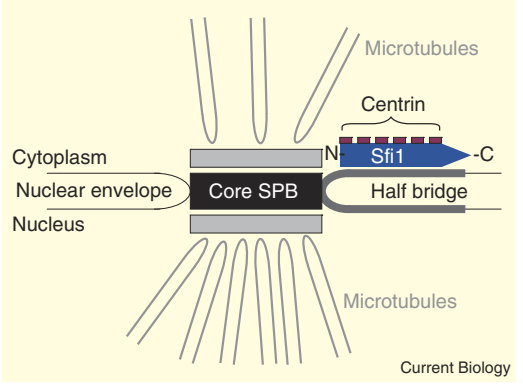

Figure 1. The Sfi1–centrin complex is positioned asymmetrically in the half-bridge of the yeast SPB.

The SPB is a trilaminar structure that lies in the nuclear envelope of the cell with microtubules emanating into the nucleus and the cytoplasm. Sfi1 (blue) with bound centrin (purple) is on the half-bridge with the amino terminus proximal to the core SPB and the carboxyl terminus distal.