Letters

Genetic Bottlenecks

The articles by Roger Lewin about genetic bottlenecks in house flies and supposed genetic bottlenecks in cheetahs (Research News, 13 Mar., pp. 1325 and 1327) may be misleading, particularly when applied to conservation genetics. For example, the impression given in Lewin's article about the house fly experiments by Bryant *et al.* (*1*) is that bottlenecks may be good for a population because genetic variance may be increased. However, according to Bryant *et al.* both viability and body size, traits positively correlated with overall fitness, are greatly reduced by the bottlenecks. In other words, these genetic bottlenecks appear to have had a rather drastic effect on mean fitness.

The basis of the apparent increase in additive genetic variance found by Bryant *et al.*, whether it is because of a combination of some rare recessive alleles and other genes with additive effects, epistasis of some sort, or a technical quirk of the experimental protocols, should be determined by directly examining these alternatives. (If a bottleneck of 16 pairs of flies had a statistically significant effect, house flies must be one of the most sensitive organisms with respect to inbreeding yet studied!) Is there some way to differentiate the additive genetic variance contributed by rare recessive alleles from that contributed by epistatic variance? Could the results of a selection experiment after a bottleneck be used to distinguish between these alternative explanations?

In the article concerning cheetahs, Lewin states that O'Brien *et al.* (*2*) concluded cheetahs are more genetically uniform than laboratory mice. O'Brien *et al.* suggest that if the supposed bottleneck occurred long ago, it would have "eliminated the most deleterious genes early in the process by natural selection." However, previous data (*3*) suggest cheetahs are not all alike, in that the infant mortality of inbred cheetah progeny is significantly higher than that of noninbred progeny. In 194 noninbred cheetahs monitored, juvenile mortality was 26.3%, while for 43 inbred progeny, the mortality was 44.2%—69% higher than in the noninbred cheetahs ($P < 0.05$). Laboratory mice generally have little inbreeding depression because brothers and sisters have been mated for many generations, thereby eliminating recessive, deleterious alleles. Laboratory mice and cheetahs may both have little electrophoretic variation, but the extent of inbreeding depression is obviously much larger in cheetahs, which suggests that cheetahs are segregating for recessive alleles affecting fitness.

The free-ranging cheetahs of the eastern African subspecies (*2*) had semen with characteristics of the captive southern African subspecies (*3*), that is, with a much lower spermatozoa count and a greater proportion of spermatozoal abnormalities than that of domestic cats. However, the semen of the two captive eastern African cheetah males tested had only 1/28 the spermatozoa concentration of that of the free-ranging cheetahs. In addition, in the sperm present, the proportion of normal sperm was only 42% of that found in free-ranging eastern African cheetahs. In other words, it appears that captive conditions also contribute to poor breeding quality in cheetahs.

Caution is the best approach when interpreting research results for application to conservation genetics. Suggesting that a bottleneck in an endangered species may be beneficial when, in fact, fitness is drastically reduced would be shortsighted to say the least. Although articles about the lack of genetic variation and bottlenecks in cheetahs are good copy, it seems to me most critical that inbreeding depression is still present in cheetahs.

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REFERENCES

1. E. H. Bryant, S. A. McCommas, L. M. Combs, *Genetics* **114**, 1191 (1986).
2. S. J. O'Brien *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **84**, 508 (1987).
3. S. J. O'Brien *et al.*, *Science* **227**, 1428 (1985).

Formation of Brown Dwarfs

W. Mitchell Waldrop's article about the possible detection of extrasolar planets (Research News, 26 June, p. 1623) by Bruce Campbell and his colleagues gives a well-balanced view of both the exciting nature of Campbell's project and the wariness of those who have also sought incontrovertible evidence of extrasolar planets. Campbell's results imply that objects with masses in the range of 1 to 10 Jupiter masses are orbiting several nearby solar-type stars, supporting the hypothesis that other planetary systems exist. Campbell also notes that companions in the range of from 10 to 80 Jupiter masses (that is, brown dwarf stars too low in mass to sustain thermonuclear fusion) can be ruled out another important finding. Contrary to what Waldrop states, however, the latter finding does not imply that brown dwarf stars do not exist. On the basis of theoretical calculations of stellar formation, binary systems composed of brown dwarfs and solar-type stars (with masses of around 1000 Jupiter masses) should be rare, and hence it would be surprising indeed if Campbell had found evidence for companions in this mass range.

Stars form from the gravitationally driven collapse of dense interstellar clouds. In order to form binary and multiple stellar systems with a wide range of separations, it is thought that clouds must fragment into protostars during the collapse phase. Theoretical calculations of the collapse phase by a number of workers who used both finite-difference (*1*) and smoothed-particle hydrodynamics (*2*) techniques have shown that fragmentation into binary systems is a common result. More important, the binary systems that form in this manner tend to have roughly equal masses, even in calculations that do not initially bias the cloud toward fragmenting into exactly equal mass binaries. This result can be understood by noting that the dominant contribution to the nonequal mass structure of binaries comes from the growth of the $m = 1$ density mode (Fourier expansion in $cos(m\phi)$, where ϕ is the angular coordinate about the rotational axis). Unlike higher order modes ($m = 2, 3 \ldots$), growth of the $m = 1$ mode is inhibited by the fact that the location of the center of mass of an isolated system must be preserved; growth of the $m = 1$ mode at one radius must be counterbalanced by $m = 1$ growth 180° out of phase at some other radius (*3*).

The theoretical prediction that newly formed binary systems should have roughly equal mass components is supported by observations of double-lined spectroscopic binaries (*4*) and solar-type contact binaries (*5*), both of which show that the initial binary mass ratio was close to unity. Mass transfer and other effects during the subsequent evolution of close binary systems may alter this initial mass ratio.

One of Campbell's best studied stars, Epsilon Eridani, is of spectral type K2 with a mass that is about 0.8 times that of our sun, or 800 Jupiter masses. If Epsilon Eridani was in a binary system, then its companion should have a mass close to 800 Jupiter masses, and hence it would not be expected to have a brown dwarf companion. The fact that Epsilon Eridani appears to be a single star surrounded by at least one object with a mass of 1 to 10 Jupiter masses is quite consistent with our present understanding of star and planet formation. Stars form

from the primary process of the collapse and fragmentation of interstellar clouds, producing objects no less massive than about 10 to 20 Jupiter masses (*6*). Planets form as a result of secondary processes in the flattened accretion disks surrounding newly formed stars. Because accretion disk masses are typically a fraction of the mass of the central protostar and a number of planets may form, planetary masses should only be a small fraction of their star's mass.

Unfortunately, brown dwarf stars probably occur primarily in isolation as single stars, or as members of brown dwarf binary systems. Because of the absence of a more massive luminous companion, these stars may well elude discovery until more powerful infrared telescopes (for example, the Space Infrared Telescope Facility) are employed in the uncertain future.

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REFERENCES

1. A. P. Boss and P. Bodenheimer, *Astrophys. J.* **234**, 289 (1979); P. Bodenheimer, J. E. Tohline, D. C. Black, *ibid.* **242**, 209 (1980).
2. R. A. Gingold and J. J. Monaghan, *Mon. Not. R. Astron. Soc.* **204**, 715 (1983); S. M. Miyama, C. Hayashi, S. Narita, *Astrophys. J.* **279**, 621 (1984).
3. A. P. Boss, *ibid.* **237**, 866 (1980).
4. L. B. Lucy and E. Ricco, *Astron. J.* **84**, 401 (1979).
5. F. van't Veer, *Astron. Astrophys.* **98**, 213 (1981).
6. A. P. Boss, *Astrophys. J. Suppl. Ser.* **62**, 519 (1986); *Astrophys. J.*, in press.

Blocked Ontogeny

I would like to comment on the statement given prominence in an article by Jean L. Marx (Research News, 15 May, p. 778): "The view that cancer results from a block in differentiation is naïve at best." No one can quarrel with the efforts by many investigators to overcome blocks in differentiation in tumor cells by using natural factors or chemotherapeutic agents. It should be made clear, however, that the concept of "oncogeny as blocked ontogeny" (*1*) was from the outset understood as "partially blocked ontogeny" (*2*). Differentiation need not be completely blocked, only blocked *enough*. The blocked ontogeny hypothesis is not naïve; it provides the only framework today for integrating ongoing experiments in developmental biology and carcinogenesis at the molecular level.

Further development of the hypothesis calls for experiments that examine the interaction of three kinds of regulatory genes (*3*). Arbitrary designations for these genes are here given as (i) the *gf*, expressed as a growth factor GF; (ii) the *sr*, expressed as a suppressor receptor SR; and (iii) the *s*, expressed as a growth inhibitor or suppressor S. Moore and his collaborators (*4*) mention a growth factor that can stimulate the cell cycle at low concentrations and stimulate differentiation at higher concentrations, and they refer to qualitative concentration effects observed by Metcalf.

The blocked ontogeny hypothesis suggests that stem cells express *gf* (or receptors for GF from other cells), but not the genes for SR or S. Differentiation leads to expression of *sr*, and *s* and may be promoted by increased levels of GF over and above those needed for growth. Partially blocked ontogeny could result from mutations in *sr* that lower affinity of SR for S or even that lead to total loss of SR. Closure of a feedback loop that would promote normal homeostatic balance between cell reproduction and differentiation might be effected by the production of second signals when S combines with SR, which would lead to decreased expression of *gf*. Recent work by Trosko and his colleagues on the role of gap junctions in intercellular communication (*5*) suggests that the appearance and function of gap junction may be a step in a homeostatic feedback loop that leads from GF to SR to S and back to *gf*.

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REFERENCES

1. V. R. Potter, *Can. Cancer Conf.* **9**, 9 (1968).
2. ———, *Brit. J. Cancer* **38**, 1 (1978).
3. ———, *Environ. Health Perspect.* **50**, 139 (1983); *Prog. Nucl. Acid Res.* **29**, 161 (1983).
4. K. Welte *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **82**, 1526 (1985).
5. C.-C. Chang *et al.*, *Cancer Res.* **47**, 1634 (1987).

Erratum: In the letter "Cancinogenicity and allergenicity" by Merril Eisenbud (26 June, p. 1613), the first sentence of the second paragraph should have read, "Two metals (Ba and Bi) are reported to be neither allergenic nor carcinogenic."

Erratum: In the article "Splicing of messenger RNA precursors" by Phillip A. Sharp (13 Feb., p. 766), the results of C. Weissmann (*53*) were incorrectly described. As H. Hornig *et al.* show [*Nature (London)* **324**, 589 (1987)], a C at the branch site of a precursor RNA does not arrest splicing at the intermediate stage, while either a U or a G at this position does arrest splicing at this point.

Erratum: The caption for the map accompanying the article "Bolivia swaps debt for conservation" by John Walsh (News & Comment, 7 Aug., p. 596) does not make clear that the land indicated remains in Bolivian ownership and will be a conservation area.