Response

The work we described in *Science* demonstrates that the induction of digit formation and the regulation of digit identity are mechanistically separable. Newman does not seem to acknowledge this distinction in his published research. He cites in his note 1 experimental studies that exclusively address the formation of limb cartilages and how digit number might theoretically be regulated; there are no informative data or commentary dealing with the regulation of digital identity or A/P asymmetry. The passage (*1*) cited by Newman is ostensibly consistent with our conclusions. However, he did not hypothesize a coherent and testable model that predicted what sort of "local interactions" might lead to "morphological nonequivalence" of limb skeletal elements.

In our report, we offered a model of how A/P positional information is organized in the developing autopod at the time that digital identity is being specified (*2*), in which the term "A/P positional information" was simply intended to reflect hypothesized molecular asymmetries that necessarily underlie the obvious morphological differences later apparent among digits. We did not intend that term to connote a strict adherence to Wolpert's conception of how positional information is interpreted, or we would have cited his work [for example, (*3*)]. We instead favor a model, influenced by work in *Drosophila* [for example, (*4*)], in which the autopodial precursors of the limb bud mesoderm are stably organized into a series of nonequivalent sectors by responding to early zone of polarizing activity (ZPA) signals in a threshold-dependent manner; these compartments later correspond to the interdigital tissues. We propose that a generic digital cartilage developmental program is activated where compartmental boundaries abut, and that digit A/P identity is subsequently specified by the flanking interdigital tissues. Economy is generally the rule in development, and our "compartmentalized autopodial mesoderm" model can simultaneously account for digit formation and specification of A/P identity, thus distinguishing it as distinctly non-Wolpertian, and non-Newmanian as well.

Randall D. Dahn
John F. Fallon
Department of Anatomy, University of Wisconsin, Madison, WI 53706, USA. E-mail: jffallon@facstaff.wisc.edu

References and Notes

1. S. A. Newman, *Trends Genet.* **4**, 329 (1988).
2. See supplemental data from our report at http://www.sciencemag.org/feature/data/1049492.shl
3. L. Wolpert, *J. Theoret. Biol.* **25**, 1 (1969).
4. D. Nellen, R. Burke, G. Struhl, K. Basler, *Cell* **85**, 357 (1996); M. A. Sturtevant, B. Biehs, E. Marin, E. Bier, *Development* **124**, 21 (1997); K. Lunde, B. Biehs, U. Nauber, E. Bier, *Development* **125**, 4145 (1998); B. Biehs, M. A. Sturtevant, E. Bier, *Development* **125**, 4245 (1998).

CORRECTIONS AND CLARIFICATIONS

Reports: "Interconnected feedback loops in the *Neurospora* circadian system" by K. Lee *et al.* (7 Jul., p. 107). In Figure 4, the leftmost circle indicating the type of feedback should have been a minus sign for negative feedback, not a plus-minus sign. A corrected (smaller) figure is shown here.