

received adequate preliminary characterization, it is doubtful that there could be many tens of martian meteorites among them. Only one meteorite, ALH 84001, has a formation age consistent with the presumed age of the southern highlands.

The inescapable conclusion is that one or more of the assumptions that go into the chain of logic outlined above are wrong. Where the error lies is unknown, but either the cosmic-ray exposure ages do not yield the launch times, or the crystallization ages are not the true ages, or a much greater fraction of the martian surface is ≤ 1300 million years old. This issue was discussed in detail by Nyquist and colleagues, who suggested a possible resolution of the paradox (1). However, the solution to this conundrum will most likely require returned bedrock samples from carefully selected terrains on Mars.

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7. The observed crater densities provide relative ages of the various surfaces of Mars. The relative ages are converted to absolute ages by using estimates of the rate of impacts and the size spectrum of impacting bodies to calculate how long it would take to build up the observed crater density. Two different absolute age scales for Mars have been developed from this method, which are the source for the estimates of $<16\%$ or $<7\%$ for the proportion of Mars's surface composed of young volcanic rock.

Fingering Digit Identity

In commenting on the study by Dahn and Fallon on digit identity in the vertebrate limb (Reports, "Interdigital regulation of digit identity and homeotic transformation by modulated BMP signaling," 21 Jul., p. 438), one developmental biologist told *Science* correspondent Michael Hagmann, "Nobody anticipated that the positional information does not reside within the digit precursors" (News of the Week, "Why chicks aren't all thumbs," 21 Jul., p. 372). In fact, for more than two decades, my colleagues and I have argued that the primary mechanism in the establishment of the limb skeletal pattern is one that establishes arrays

of equivalent elements (for example, digits) that are individualized at later stages by means of local interactions. We have supported our arguments by studies of limb bud tissues in vitro and by theoretical models (1). In a 1988 minireview (2), we noted that a solution to the developmental problem of limb pattern formation would be to "consider the various skeletal elements as equivalent from their inception...[This] places greater emphasis on the similarities between the various skeletal elements than on their differences when considering the mechanisms that first establish them as skeletal elements. If the various elements are eventually to become nonequivalent morphologically, biochemically, or physiologically, these differences could be acquired by local interactions that lead to second order modifications of the original pattern."

One obstacle to understanding the underlying mechanisms of skeletal pattern formation is the notion of "positional information" itself. Positional information has been proposed to be embodied in a molecular gradient that provides an address for each cell in an embryonic field (3). As regards the limb, this theory hypothesizes that each skeletal element to be generated requires a distinct cellular

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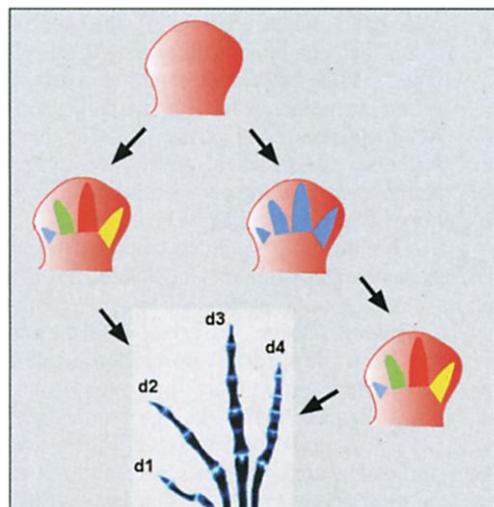
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differentiation pathway or developmental program (4). Although every cell might follow any one of these pathways, any particular cell has been considered to be capable of responding to the level of the gradient it experiences by developing into the positionally appropriate skeletal element. The positional information hypothesis predicts that the various skeletal elements are nonequivalent from their inception, contrary to what has now been

found by Dahn and Fallon. Since this hypothesis was first presented, the corresponding gradient in the limb bud has successively been proposed to be retinoic acid or its receptors (5), *Hox* gene products (6), and Sonic hedgehog protein (7). None of these has proved to be a factor that elicits distinct skeletal elements at different concentration values.

The new observations by Dahn and Fallon essentially falsify positional information as an explanatory model. Yet, although the authors conclude that the limb's digits arise as equivalent structures that are customized by local influences later in development, they



Possible pathways of digit formation.

In the "positional information" scheme on the left, the gradient constitutes a coordinate system in reference to which limb bud mesenchymal cells form digits with distinct identities from the start. In the "isomorphic prepattern" scheme on the right, digits are initiated by a spatially periodic common signal, making them originally identical and the molecular gradients customize the digits after they begin to form. (Victoria blue-stained cartilaginous skeleton of embryonic chicken leg, with digit identities denoted, adapted from Fig. 1A of Dahn and Fallon's report.)

still discuss their results in terms of "A/P [anteroposterior] positional information" despite the lack of evidence for or any reason to expect that the primary mechanism generating multiple equivalent digits or the secondary system of local mediators of digital identity constitute the sort of global map hypothesized by the positional information model.

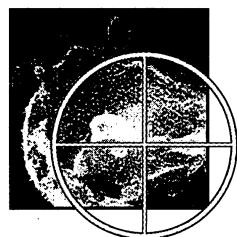
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Response

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 po-

sitional 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.

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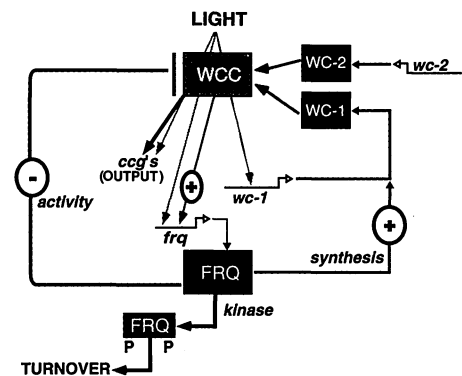
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CORRECTIONS AND CLARIFICATIONS

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.



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