ter at Duquesne University. In that regard, I welcome the comments, suggestions, and cooperation of scientists everywhere who share these views.

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Village Solidarity

Peter Suzuki [*Science* **132**, 891 (1960)] makes a most important point and one which I had almost despaired of seeing in a "neutral" journal—that of "village solidarity." While he may overstate the case by saying that what "is generally taking place in many of the underdeveloped countries is a ruralization of the cities. . ." (since the majority of these cities were hardly urban within the meaning this term has assumed in recent years), yet it must be stated repeatedly that, with few exceptions, aid administrators continue to err in failing to recognize that this group attitude is a prerequisite if their rural programs are to meet with success. The opposite view, held in the past and still the principal method of assistance—that this sense of common identity and common purpose must be altered or eradicated before change can take place—has resulted in the almost unqualified failure of rural development programs carried on by the International Cooperation Administration and its predecessors throughout the so-called "underdeveloped nations." I am therefore quite happy that Suzuki has supplied us with an additional case study to substantiate my criticism of the direction these programs have taken. ["*Social and political aspects of Philippine economic development*," Philippine Council, Institute of Pacific Relations (Kyoto Conference, Pacific Council, Institute of Pacific Relations, 1954) (mimeographed)].

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Developmental Selection of Mutations

We should like to comment on the interesting and provocative report by L. L. Whyte entitled "Developmental selection of mutations" [*Science* **132**, 954 (7 Oct. 1960)]. Whyte is well known as a perspicacious and imaginative thinker and, as always, his writings are worthy of consideration. If we understand his report correctly, however, the problem to which he alludes does not really exist.

Whyte's main point seems to be that there is a class of mutations whose role in evolution has not been appreciated by students of the evolutionary process. These are the mutations which prevent "internal organizational efficiency permitting continued growth." In other words, he is referring to lethal and detrimental mutations whose effect is manifest during morphogenesis, as opposed to those genes whose morphogenetic effect is to produce an adult ill-adapted to the adult environment. We are rather aghast to learn that a perusal of the literature has left Whyte with the impression that such genes have been neglected. The existence of a very large class of embryonic lethals is very well known to evolutionists and geneticists in general. Elementary textbooks of population genetics always begin by a discussion of gene-frequency changes in populations, in which unconditional lethals are segregating, before going on to the discussion of more subtle forms of natural selection [see, for example, C. C. Li's textbook, *Introduction to Population Genetics*]. If general works on evolution fail to deal explicitly with such lethal genes, it is largely because they *are* so well known that it hardly seems worthwhile calling further attention to them. As a matter of fact, Lewontin and Dunn have recently published [*Genetics* **45**, 706 (1960)] a report on the evolutionary dynamics of a series of unconditional embryonic lethals in wild populations of *Mus musculus*.

There is, however, a more subtle and more important point here. Students of evolution have emphasized the interaction of environment with genotype because they have for some time realized that there is no real distinction between "developmental selection," as Whyte so aptly calls it, and postembryonic adaptation. There is no sharply defined boundary between unconditional embryonic lethals and those whose effect is intimately bound up with environment. There is, rather, a continuous spectrum of gene effects, from those genes whose action seems virtually independent of any environmental modification, to those whose sensitivity to environment encompasses every slight change of physical and biotic milieu.

We would venture so far as to say that no gene is totally independent of environment in its expression, and therefore the fitness of every genotype is in some measure a function of environment. It is, of course, true that early embryonic lethals whose effect is to completely disrupt the normal morphogenetic pattern to the point of death are less susceptible of modification. But they are not wholly insensitive to it. In general, the more protected

the embryonic tissue is against changes in the milieu, the more unconditional will be the lethality. No one has yet found an environment in which the *t* alleles in the mouse are viable as homozygotes, but in *Drosophila* there are many genotypes that are complete preimaginal lethals at one temperature yet viable at another.

Human disorders such as erythroblastosis foetalis and diabetes mellitus trace back to primary metabolic processes, yet man has created environments in which such genotypes survive. Even for early embryonic lethals in mammals it is reasonably certain that these lethal effects can be traced to some enzymatic imbalances. Presumably the molecules that are missing could be supplied exogenously, perhaps simply by ingestion of food of the right kind. We know very well that even very large protein molecules such as antibodies can pass across the placental membranes. In general, the degree to which the fitness of various genotypes will depend upon the environment is related to the time of action of the genes in development and the proximity of the phenotypic result to the primary gene action. Yet, even when the effect is proximate to the primary gene action, environmental modification must be reckoned with. Thus, there are mutants in *Neurospora* which block single steps in known enzymatic reactions, but whose effects are sensitive to temperature.

Finally, it should be pointed out that geneticists in fields other than evolutionary study have quite deliberately chosen to work with genes that are insensitive to environmental modification. Investigations of the physicochemical nature of the genes are made very much easier by eliminating the confusing effects of environment, just as the early elucidation of the fundamental laws of classical genetics was made possible by the deliberate choice of environmentally insensitive traits.

What Whyte's report suggests is that nongeneticists have not yet fully comprehended the concept of the "norm of reaction." A careful rereading of the first chapter of Schmalhausen's *Factors of Evolution* might be in order. Organisms at every stage of their development are the products of heredity and environment. To maintain any other position is to ignore the overwhelming weight of fact and reason.

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R. C. Lewontin and E. W. Caspari's courteous and informative letter neglects the main issue and is on one point misleading.

The developmental elimination of

harmful mutations has long been studied. This may be called "negative developmental selection"; it produces no evolutionary change, and was discussed only to provide the background to "positive developmental selection." The constructive thread of my argument concerned evolutionary change, this term or an equivalent being used five times. Such change involves positive developmental selection, the preservation of neutral or favorable mutations which, because they conform to the necessary conditions of biological organization in the particular species and therefore survive developmental selection, may determine the direction of evolutionary change—for example, in periods when there are no significant changes in the environment. This is now being studied in a few special fields, but no general inferences regarding these still unknown conditions are yet possible.

The authors, occupied with my assumed ignorance of work on lethals (though deliberately mentioned), seem momentarily to forget that "selection" does not merely mean "elimination" and do not mention evolutionary change! I am grateful; this proves there was a flaw in my exposition; the term "positive developmental selection" is necessary, much current experimental work being on elimination. N. B. Schmalhausen (1949) does not mention positive developmental selection.

The concept of positive developmental selection, already expressed by Dobzhansky [*Genetics and the Origin of the Species* (Columbia Univ. Press, New York, 1937)], Haldane [in *Darwin's Biological Work*, P. R. Bell, Ed. (Cambridge Univ. Press, Cambridge, 1959), p. 147], and possibly others, merits attention. Hence my report. If genetic systems or developmental processes or, more broadly, the conditions of biological organization in the species ever determine the actual, or restrict the possible, direction of evolutionary change, then the now prevailing form of the theory of evolution by adaptive selection and its mathematical expressions are likely to require modification —that is, generalization to include the very different effects of developmental selection.

If the term "developmental selection" is "apt," and the work cited by the authors is relevant, then the problem of developmental selection must "really exist."

This inconsistency arises from a *non sequitur*. It is not correct, as Lewontin and Caspari seem to suggest at one point, that the principles, (i) that internal and external factors interact in some degree at all levels and (ii) that organisms at every stage are products of heredity and environment, make the

problem unreal by preventing the influence of the two classes of factors ever being separated. As they well know, it is normal scientific method in this cosmos of pervasive interactions to restrict the variables so that one thing can be studied at a time; indeed they give an example of this. If there is a continuum of effects the extreme cases are the most important, because simpler. To study positive developmental selection, stimulate mutations but keep the environment constant and observe what evolutionary changes occur, or examine corresponding situations in the past. And on the theoretical side it may one day be possible to predict the class of mutations which is capable of surviving developmental selection in a given species in a constant environment.

Other geneticists, mainly interested in negative developmental selection in microorganisms, have been surprised to discover that ideas vaguely taken for granted for some time have seldom been made explicit in the literature, and that their implications, being radical, have never been developed. [However, see J. Marquand Smith, *Theory of Evolution* (Penguin, Harmondsworth, 1959), for one of the first statements of these ideas in the literature on evolution reaching a wider audience.]

Developmental selection is of great importance, not only for evolutionary theory, but because it may hold clues to the nature of biological organization in general, at each level and in all species, which is the main problem of structural biology. The present condensed analysis is certainly imperfect; not only are the known facts inadequate, but even as a speculative theoretical statement it requires further development.

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Grants and Scientific Freedom

Norman Kaplan's recent article on "Research overhead and the universities" [*Science* **132**, 400 (12 Aug. 1960)] is certainly timely. It seems to me, however, that he has skirted one of the major aspects of the problem.

He gives as one of the three major functions of a university the "extension of knowledge." Traditionally this extension is to be directed exclusively by the university and especially by the individual investigator. Any erosion of this freedom of direction constitutes external "control" and, if it is to be acceptable at all, must be compensated by some very real gain to the welfare of the public. Kaplan has, I think, recognized this in restricting his discussion