McGill

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Dear Victor

Thanks for yours of the 6th.

You flatter me by assuming that I may be of some help in solving the problem of curing a sickness by gene substitution. However, I'll share my thoughts with you, well knowing that they are few and perhaps worthless.

1. The concept of linearity makes rigorous sense only in reference to mathematical models involving, say, differential equations. For example, whereas

$y'' + ay' + by = 0$ is linear, $yy'' + axy' + by^2 = 0$ is not .

Hence, if y_1 and y_2 are solutions of the first, their linear combination $c_1y_1 + c_2y_2$ is a solution as well, whereas no such superposition of solutions holds for the nonlinear case.

2. However, I suppose that one can transpose the previous concept to a qualitative discussion of complex systems. One may, e.g., stipulate that a system is linear if and only if a change in its composition or in its environment does not alter radically its properties. In ordinary parlance: A system is linear iff more of the same (internal reconfiguration or external perturbation) does not result in a change in kind. Even simpler: A system is linear if alterations in some of its variables or parameters does not cause it to transform into a member of a different species.

3. If the previous definition is adopted, then a gene substitution, a qualitative change, is likely to bring about some radical changes in a nonlinear system--unless the genes concerned are of the junk kind. In other words, the therapeutic effect of gene substitution is not surprising precisely because organisms are nonlinear systems (in sense 2 above).

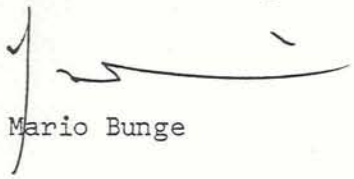
4. The mechanism of such radical changes is obvious. If one gene is substituted for a different one, then the organism will (a) start producing proteins, in particular enzymes, that it did not produce before, (b) stop producing proteins, in particular enzymes, that it used to produce, and consequently (c) undergo new chemical transformations, as well as stop hosting certain other chemical reactions.

5. Within bounds, i.e. within a certain (narrow) interval of the variables at play, certain internal changes (e.g. spontaneous gene mutations, spontaneous or non-stimulus bound neuronal discharges, etc.)are context-independent, i.e. not caused by environmental changes.

Finally, I share your views concerning the formula "Performance = Heredity + Environment + HxE interaction". Coincidentally, I was criticizing this formula in class last week. I do not understand what is meant by "interaction" in this

case. All one may say, I suppose, is that environmental factors may favor or inhibit gene expression. But this would be a one-sided action of the environment upon the genome.

Best to both of you.



Mario Bunge

P.D. Applied scientists and technologists know that, in many cases, exceedingly small "impurities" cause desirable effects. Examples: semiconduction and luminiscense. And chemists know that the substitution of one atom for another, in a molecule, usually gives rise to a compound with very different properties.. This is particularly the case with pharmaceutical products.