What does the word interplay mean? Thanks mostly to Sir Michael Rutter, the author of this characteristically systematic and comprehensive volume, the phrase gene-environment interplay has become the flavor of the month in developmental behavior genetics, but I have never seen the term defined in either a statistical or a psychological context, and Rutter does not do so, at least not formally.

It is clear enough what Rutter means by the term, however. Rutter's thesis in this book is that the resolution of the hoary nature-nurture debate is to be found in correlations and interactions among genes and environments in the genesis of behavior. It is true, as behavior geneticists have insisted for decades, that genes influence all behavior, including complex human behavior, and it is at least somewhat true that the extent of this influence can be quantified via the typical twin, adoptee, and otherwise familial research designs of the behavioral geneticist and the usual variance partitionings of the population geneticist, including the much maligned coefficient of heritability, $h^2$. But any expectations that the genetics of behavior would lead to straightforward genetic accounts of normal or disturbed behavior have not come to fruition. Genes always exert their effects in interaction with the environment and with each other, and those effects can only be observed at the outcome of the nonlinear, uncontrolled developmental process that is a human life. This outcome may be dissatisfying for committed hereditarians, naive environmentalists, and hard-core reductionists (all rare birds nowadays), but from the point of view of describing what is going on, it is a treasure trove, an endlessly renewable source of interactions and correlations, regressions, associations, and linkages to be
modeled and documented.

The book is not directed at a general nature-nurture audience, as in the style of Pinker's (2002) *The Blank Slate: The Modern Denial of Human Nature*. It is more in the style of an *Annual Review* chapter, and a good one, to be appreciated by practitioners of the trade. It would make an excellent starting point for a syllabus on nature and nurture. Rutter's rhetorical tone on the nature-nurture dimension is opinionated but unfailingly moderate, without tolerance for hard-liners on either side of the old debate, and unfailingly optimistic. We might have headed down some blind alleys in the past, but now that we have begun to grasp the complexity of things, particularly now that we have latched onto gene-environment interplay as our paradigm, we are starting to make some real progress. In fact, the interplay literature is exploding.

It is in the documentation of the byzantine stuff of social science that Rutter is at his very best. No one in developmental psychology or psychiatry can match his ability to wade into the journals and emerge with enumerations of empirical findings, methodological rules of thumb, interesting new trends, and sensible warnings about future difficulties that have not yet been anticipated. In general, I would rather read Rutter than the studies themselves, and that includes my own studies. The experience of reading the book reminded me favorably of a visit to a large museum, filled with such a huge variety of objects to admire that it winds up numbing the mind. With Rutter we take the guided tour, accompanied by a sensible companion who calls our attention to the important details and points out unseen connections between objects in different wings. We emerge focused and refreshed.

But Rutter offers no grand theories, despite the book's bold subtitle. (Typing the word *explained* into a bookseller's search field reveals that claims of comprehensive explanation of esoteric subjects are something of a trend in nonfiction book titling, the intellectual's equivalent of easy weight loss or a quick buck.) Indeed, as the book proceeds from one form of interplay to another, from the ambiguities of heritability to the difficulties of interpreting environmental risk, from genetic effects that depend on environments to environmental effects that depend on genes and to genes and environments that depend interactively on each other, as the exegesis of complexity reveals only greater complexity, one may find oneself wishing for the big, comprehensive explanation that the title promises but that Rutter is finally too wise to attempt. Even under Rutter's guidance, social science offers us one of the gifts of natural science but never the other: We are given the pleasure of seeing the small parts of intricate systems described meticulously but denied the great, transformative moment when a new insight snaps the inchoate into focus, changing our view of the world forever. The explanation of nature-nurture is that there is
no explanation; there is only interplay all the way down, a bottomless fractal that can be described locally but thwarts all attempts at comprehensive explanation. That returns us to the question: What exactly is interplay?

Like psychology more generally, modern behavioral genetics has its origins in the domain of experimental science, particularly animal breeding. The science of animal breeding has one key characteristic that sets it apart from much of what we recognize as human behavioral genetics today: randomized experimental control. The reason random assignment is the bedrock of the scientific method is that it ensures that experimental conditions are independent of other factors, especially that they are independent of each other. In the controlled context of clones in cages, genes and environment are independent, and many of the seemingly irresolvable controversies of developmental behavioral genetics make relatively good sense. Heritability, for instance—to the extent that the variability of genes and environments were under the control of the animal breeder, it made sense to attribute proportions of variability in outcome to one experimental factor or the other, and these proportions could be tied unambiguously to changes in the experimental outcome. No one would have been interested in the heritability of milk production in cows if knowledge of it was not helpful on the working dairy farm. But in the wild, where the variances of genes and environments are random and correlated, heritability is a much less meaningful concept, as it depends crucially on how the population variances are sampled. A behavior geneticist worrying about the true heritability of extraversion is like a social psychologist worrying about the true F statistic of the fundamental attribution error: It depends on how the experiment is conducted.

Fortunately, little of this book is taken up with the tired debate about heritability coefficients. Instead, it is mostly concerned with the related and equally misunderstood concept of interaction. Interaction is many-faceted. It can refer to an intuitive biological notion, in which two ingredients must come together before something can happen, conception being the obvious example. Alternatively, interaction can refer to a statistical phenomenon in which multiplicative relations among predictors are used in regression models. Suppose you have two risk factors that can take values of zero or one. If you add the factors together, both have equal weight, and the result can take values of zero, one, or two, quantifying the additive amount of risk. But if you multiply the predictors together, the only possible results are zero and one, the one occurring only when both risks are present.

Thus, there is an analogy between causal interactions and statistical ones. The relation between them is looser than it might appear, however, and, as Rutter notes, there is a history of controversy about the conditions under
which the former can be inferred from the latter. (Eaves, 2005, e.g., showed that statistical interactions between measured genes and environments, the kind of result widely cited by Rutter, are easy to simulate using processes that have little to do with biological interactions of genes and environment.) But, for once, Rutter's impeccable pedagogical skills fail him at this crucial juncture. He never really explains the inferential problem (which is essentially that the presence of statistical interaction depends crucially on how predictor variables are scaled) in any detail. He basically asks the reader to trust him and gets back to the main task of summarizing interesting studies of gene-environment interplay. Most readers will not notice the omission of what seems like a technical matter of statistics.

But the ambiguities of interaction do matter, in ways that cut deeper than Rutter may appreciate. Like heritability, interaction was a relatively tractable idea in the heyday of 2 × 2 analysis of variance, with participants assigned at random to fixed conditions. There were two main effects and one interaction independent of the main effects, and if testing of the interaction was more dependent than one might like on the measurement scale of the outcome, well, at least the number of predictors was limited and the variances were under experimental control and therefore independent of each other and their interaction.

As usual, out in the big, uncontrolled world, everything gets harder to tie down. The typical field study of exposure to naturally occurring environments includes hundreds of variables, all of them potential predictors and outcomes, all correlated with each other, all probably causing each other, most of them completely outside the experimenter's control. Plausible but ultimately arbitrary decisions get made about what is considered y and what is considered x, some ad hoc model is fitted to the convoluted multivariate structure of the data, and if the researcher is skilled, something like a story line emerges. Does that story line represent an actual, replicable, causal sequence that is responsible for the phenomenon of interest? It is best not to ask, and we generally do not. But to us aficionados of social science, it is interesting anyway, for better or for worse it is what we do, and, when interpreted by a critic as discerning as Rutter, it can become coherent and even enlightening.

By contemplating the future of psychological genetics at the outer limits of the scientific method, Rutter is entering a philosophical discussion of the relation between natural science and the nonexperimental social sciences, a tradition highlighted by the classic articles of Cronbach (1957) and Meehl (1978). It is unfortunate that Rutter does not acknowledge the more explicitly philosophical aspects of his topic, because, ultimately, the questions he is posing cannot be answered by empirical studies alone.
When you add DNA, nature's very paradigm of variation, to the hundreds of variables in that environmental risk study, the number of potential predictors doubles, and the number of interactions gets raised to the next power, into the hundreds of thousands and beyond. Everything interacts with everything, and the possibilities for discovering interesting social scientific results exponentiate even as the probability that any of them will replicate as a meaningful scientific hypothesis dwindles to nullity. The term of art for the proliferation of these uncontrolled correlations and interactions, and the corresponding abandonment of hope for a replicable relation between statistical and biological reality, is interplay.

Interplay is interaction that has gotten out of its cage. Interplay is what happens to medical genetics when it finds itself in a world of ethics and will. Interplay is the difference between brass-instrument analysis of variance and structural equation modeling. Interplay is the difference between biology and psychology, between drosophila and people, between natural science and social science, between the domesticated and the feral, between replication and diversification, between cumulative technology and expressive play. Interplay is science becoming narrative, and then finally—please keep this quiet, the NIH doesn't know—sprouting wings and taking flight as literature.

References


