Guidelines for DNA Hybrid Molecules

Those in attendance at the 1973 Gordon Conference on Nucleic Acids voted to send the following letter to Philip Handler, president of the National Academy of Sciences, and to John R. Hogness, president of the National Institute of Medicine. A majority also desired to publicize the letter more widely.

We are writing to you, on behalf of a number of scientists, to communicate a matter of deep concern. Several of the scientific reports presented at this year's Gordon Research Conference on Nucleic Acids (June 11–15, 1973, New Hampton, New Hampshire) indicated that we presently have the technical ability to join together, covalently, DNA molecules from diverse sources. Scientific developments over the past two years make it both reasonable and convenient to generate overlapping sequence homologies at the termini of different DNA molecules. The sequence homologies can then be used to combine the molecules by Watson-Crick hydrogen bonding. Application of existing methods permits subsequent covalent linkage of such molecules. This technique could be used, for example, to combine DNA from animal viruses with bacterial DNA, or DNA's of different viral origin might be so joined. In this way new kinds of hybrid plasmids or viruses, with biological activity of unpredictable nature, may eventually be created. These experiments offer exciting and interesting potential both for advancing knowledge of fundamental biological processes and for alleviation of human health problems.

Certain such hybrid molecules may prove hazardous to laboratory workers and to the public. Although no hazard has yet been established, prudence suggests that the potential hazard be seriously considered.

A majority of those attending the Conference voted to communicate their concern in this matter to you and to the President of the Institute of Medicine (to whom this letter is also being sent). The conferees suggested that the Academies establish a study committee to consider this problem and to recommend specific actions or guidelines, should that seem appropriate. Related problems such as the risks involved in current large-scale preparation of animal viruses might also be considered.

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Behaviorism and Feedback Control

Although there is much of value in the article "Feedback: Beyond behaviorism" by W. T. Powers (26 Jan., p. 351), it is based on an outdated and misconceived idea of behaviorism.

Behaviorism consists in the view that a scientific psychology must deal with the observable. From this proposition, it follows that psychology should be a science of behavior, and that explanations of observed phenomena should be couched in the same terms as the observations themselves, rather than invoking imagined autonomous entities ("explanatory fictions") as causes. Many, perhaps most, psychologists today are behaviorists.

Since its points are mainly methodological, behaviorism never has been wedded to any particular conception of behavior. Early behaviorists perhaps held views similar to the one Powers criticizes, but the inadequacy of describing behavior in terms of responses to stimuli was recognized over 30 years ago. With the recognition that behavior is affected by its consequences (the Law of Effect), open-loop descriptions began to pass away. Few behaviorists today would disagree with Powers's statement, "there can be no nontrivial description of responses to stimuli that leaves out purposes." Emphasis on purpose, in fact, has been the hallmark of modern behaviorists' thinking (*1*). The behaviorists' solution to the problem of purpose has been exactly the one suggested by Powers—selection by consequences. That behavior and consequences constitute a feedback system is taken as a basic premise (*2*). It is presented this way in at least one elementary text (*3*).

Powers covers familiar ground in two other points. In his discussion of acts and results, he actually reinvents Skinner's concept of the operant (*4*). One of Skinner's most important innovations was this conception of a unit of behavior consisting of the class of responses (Powers's "acts") defined by its environmental effect (Powers's "result"). As Herrnstein has pointed out (*1*), Skinner's approach to the problem of purpose was to define behavior in terms of its consequences. Also familiar is the notion of the hierarchical organization of behavior. Lashley (*5*) made the earliest clear statement of this view. He argued, as does Powers, for a hierarchy of goals and subgoals in behavior. It seemed the only way to account for organized sequences.

Although Powers's attack on behaviorism is misguided, and many of his ideas have been set down before, nevertheless the constructive aspects of the article deserve praise. The very lack of novelty itself shows that Powers, albeit unwittingly, is square in the mainstream of modern behaviorists' thinking about instrumental behavior. His discussion of feedback, therefore, is most welcome, because it helps define the direction in which we are moving.

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References and Notes

1. R. J. Herrnstein, introduction to J. B. Watson, *Behavior* (Holt, Rinehart, and Winston, New York, 1967).
2. The opening sentence of *Schedules of Reinforcement* by C. B. Ferster and B. F. Skinner (Appleton-Century-Crofts, New York, 1957) reads, "When an organism acts upon the environment in which it lives, it changes that environment in ways which often affect the organism itself."
3. H. Rachlin, *Introduction to Modern Behaviorism* (Freeman, San Francisco, 1970). See also D. J. McFarland, *Feedback Mechanisms in Animal Behaviour* (Academic Press, London, 1971) and P. van Sommers, *The Biology of Behaviour* (Wiley, Sydney, 1972).
4. B. F. Skinner, *The Behavior of Organisms* (Appleton-Century-Crofts, New York, 1938). See J. R. Millenson, *Principles of Behavioral Analysis* (Macmillan, New York, 1967) for a treatment in terms of set theory.
5. K. S. Lashley, in *Cerebral Mechanisms in Behavior*, L. A. Jeffress, Ed. (Wiley, New York, 1951), p. 112.

Powers briefly describes a closed-loop feedback model of behavior, with special reference to purposive behavior. The model is of interest and deserves serious consideration as an alternative to other behavioral models, but there are some points about the presentation that warrant critical comment.

First, as a model, the system can do no more than *represent* the phenomena in the domain encompassed. A model (of the type under consideration here) provides no explanations, except in the sense of intuition or analogy. Powers does not describe the theory to be associated with the model, and therefore no real explanations are provided.

Second, Powers asserts that no behavioristic model has been able to account for purpose; but in fact purpose has been adequately derived from such behavioristic constructs as the conditioned goal response (the fractional anticipatory goal response, r_g) and other mediational response. In Powers's system, "purpose" is like a template; its effect is not goal-seeking behavior but goal-maintaining behavior, and it is concurrently represented in

the system. Powers does not provide adequate, empirically based definitions of the key concepts, such as "reference signal," and in this sense his model is nonbehavioristic. Nevertheless, as far as one can determine, the model is mechanistic, in that the components of the feedback loop are analyzed as a unidirectional, linear causal chain. The very fact that the components can be analyzed in this way indicates that there is no dialectic interpenetration, or reciprocal interaction, because in such interactions the components are inseparable from the whole or structure that comprises them (*1*).

Powers concludes that "Behavior itself is seen in terms of this model to be self-determined in a specific and highly significant sense that calls into serious doubt the ultimate feasibility of operant conditioning of human beings." Were it not for the ambiguity of the meaning of "ultimate feasibility," one could reject the statement on empirical grounds. The research literature is replete with studies demonstrating operant conditioning in human subjects by human experimenters, in some cases without the subjects' being aware even that they were subjects (*2*). One can also, in any case, question the statement on theoretical grounds, because "self-determined" has, as Powers says, a specific meaning in the model, and this meaning has no implication of free will. In the model, "organisms are self-determined in terms of inner control of what they sense, at every level of organization except the highest level." Inner control refers to feedback ("error signal") regarding the discrepancy between the "reference signal," or goal, and the "sensor signal," or input. As the model is mechanistic, the error signal will inexorably produce specific "effector functions," or responses. That is, the responses are completely determined by the error signal (and, perhaps, by the state of the system), and the error signal is completely determined by the reference signal and sensor signal. As the sensor signal is determined by the environment, any variability in self-determination must come from variability in reference signals. Their source is not specified in the model (except at the highest level, at which they are assumed to be biogenetically determined). The model does not demand a reference signal that prohibits operant conditioning; this reference signal was introduced ex hypothesi and is not entailed by the model.

In summary, the model (i) is not explanatory, (ii) is not the only mechanistic model that provides a derivation of purpose, and (iii) does not intrinsically preclude human operant conditioning.

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References

1. H. W. Reese and W. F. Overton, in *Life-Span Developmental Psychology: Research and Theory*, L. R. Goulet and P. B. Baltes, Eds. (Academic Press, New York, 1970); pp. 115–145; W. F. Overton and H. W. Reese, in *Life-Span Developmental Psychology: Methodological Issues*, J. R. Nesselroade and H. W. Reese, Eds. (Academic Press, New York, 1973), pp. 65–86; W. F. Overton, *Hum. Develop.*, in press; L. von Bertalanffy, *General System Theory* (Braziller, New York, 1968).
2. H. M. Rosenfeld and D. M. Baer, *Psychol. Rev.* **76**, 425 (1969).

The comments by Baum and Reese on my control-system approach to understanding behavior are the most balanced I have received from behaviorists. I thank them for trying to find a place for my work within behaviorism, an attempt that reflects generosity, but not understanding, of what I said (or tried to say). The conceptual basis of control-system theory is so alien to behavioristic thought that there can be no such easy reconciliation. The best we can hope for is a constructive confrontation.

Baum says that a scientific psychology must deal with the observable, which to him means behavior. Behavior, however, is not something self-evident that anyone can see just by looking. What is the behavior of a man walking? Is he really tensing his leg muscles, moving his legs, walking, going to buy a paper, on his way to work, making a living for his family, or maintaining his self-respect? The point of view of the observer defines the behavior he sees. The *actual* behavior of the nervous system consists only of sending neural signals to muscles and glands; that is the last event that truly reflects the system's output. From that point outward, the results of that output become more and more mixed with properties of any events in the external physical environment, so that even such elementary behavior as a "movement" no longer is a unique indicator of a particular activity in the nervous system. Thus, while Baum's pronouncement seems reasonable on the surface, it ignores one of the deepest conceptual dilemmas of behaviorism.

The control-system model shows that behavior at any level, as well as its relationship to "stimulus events," makes sense as soon as one recognizes the

concept of the controlled quantity. To find the proper definition of the controlled quantity, the observer must recognize that his own point of view determines the behavior he will observe, and he must find an objective way to discover the *right* point of view —namely, that of the behaving system. The observer must try to find out which of the infinity of potential controlled quantities is the one that the behaving system is actually sensing and controlling. Only when the controlled quantity has been correctly identified can the observer see that the system's outputs are always such as to counter the effects which environmental disturbances would otherwise have on the controlled quantity. In my article I presented an experimental paradigm, new to psychology, for testing hypotheses concerning the controlled quantity and its reference level.

In the section on controlled quantities in my article, there appears an approximation, $g(d) \approx -h(o)$, which says that the cause-effect relationships that can be observed between stimulus events and consequences of nervous system outputs—responses—are expressible wholly in terms of the physics of the local environment, containing almost no information about the behaving system at all. I see no way in which behaviorism can survive a full understanding of the derivation and significance of this harmless expression. If control-system theory does indeed describe correctly the relationship between organisms and their environments, behaviorism has been in the grip of a powerful illusion since its conceptual bases were laid.

It is therefore not possible that behaviorism already contains an adequate treatment of feedback phenomena; if it did, a behaviorist would have discovered this illusion already. Many behaviorists have observed feedback phenomena, but they have tried to deal with them by translating the terminology of control-system theory in such a way that well-accepted behavioristic principles would remain undisturbed. That is why "purpose" has lost its original meaning of inner purpose or intentionality, and has been redefined as *consequences*. That redefinition was necessitated by the fact that early behaviorists knew of no physical system that could contain inner purposes—their telephone-switchboard model had no place for them, and control-system theory then lay far in the foreseeable future.

In control-system terms, a purpose

is not a consequence of behavior, but a model inside the organism for what it wants the perceptual consequences of its outputs (modified by environmental disturbances or not) to be. When I bowl, my inner purpose is to perceive all the pins falling on the first ball. What I perceive is generally something different. I am still doing my best to alter my outputs in such a way as to reduce the error between what I generally perceive and what I intend to perceive. Another observer can discover that intended perception by manipulating my environment until he finds the state where I cease to alter my outputs in opposition to the changes he causes. There is nothing metaphysical or conjectural about this process. But it does not make any sense in behavioristic terms, because it is designed around rigorous laws of feedback, not around the imprecise usages of the term feedback that are found in behaviorism.

There seems to be a general impression that feedback is analyzable (in Reese's terms) by following a "unidirectional, linear causal chain" around and around a closed circle (I trust that Reese noticed that the circle *is* closed). That approach to feedback, often expressed as taking into account the effects of a response on subsequent stimuli, is the natural one, but, as every beginning control-system engineer soon discovers, it leads to totally incorrect predictions of the behavior of the system being modeled. The qualitative chain-of-events approach leaves out the crucial factor of system dynamics; when that is properly taken into account, through use of a physical analysis of the system and its environment and application of differential equations or transform methods, a very different and surprising picture emerges. If the control system one wants to model is free of spontaneous, self-sustained oscillations (as normal behavioral systems are), time lags in the system can safely be ignored, and the behavior of the whole system can be seen quite correctly as occurring *simultaneously* with disturbances. The output changes *along with* the disturbance (a normal, slowly varying disturbance), and the input variable being monitored continually tracks the inner reference signal, if a variable inner reference signal exists. There are no loopholes in this analysis; if organisms are in the negative feedback relationship with their environments, this is how they behave. To arrive at a different conclusion, one would have to show that the bases of

control-system theory are wrong, and he would have a lot of engineers who use it every day to convince.

Thus, the attempts by behaviorists to bring feedback phenomena into the scope of their conceptual scheme have involved only a superficial adoption of certain terms and loose qualitative observations, the true beauty and power of control-system concepts having been left behind. The distortions of feedback theory that occurred in the adoption of the terminology were precisely those which would prevent change in the basic conceptual scheme of behaviorism (this should not surprise control-theory fans, since all organisms manipulate their own perceptions to keep them in the desired state).

There is no "reference signal that prohibits operant conditioning," as Reese puts it while guessing wrong about what I meant. Operant conditioning is a fact; in my model, it is a portion of a control process whereby organisms modify their own inner structure of control systems as a means of keeping certain critical variables (W. R. Ashby's term, as I noted), at genetically established reference levels. I was talking about the *feasibility* of people deliberately trying to control the behavior of other people through deliberate application of operant conditioning.

In order to control another person, one must establish contingencies or schedules of reinforcement. Whatever one chooses to use as a reward, he must make sure (i) that the subject needs or wants the reward and (ii) that the *only* way the subject can obtain the reward is by doing what the experimenter wants to perceive him doing. The experimenter, of course, is trying to control his own perceptions relative to his own inner purposes, using the subject as his means.

The establishment of contingencies, therefore, requires that the experimenter already be the sole source of something the subject wants, and establishing that situation is where operant conditioning will fail as a way of controlling behavior—as it has failed throughout recorded history. An experimenter trying to control people rather than laboratory animals cannot conceal the fact that he has what the subject wants, and is withholding it until the subject does what the experimenter demands. If one person can establish a contingency, another person can see that he has done so, and can decide to "unestablish" it. If the act that the experimenter wants to see performed in any way inconveniences the subject, the subject will be forced by his own nature to find a way to circumvent the contingency. He can operate properly only on the basis of his own inner purposes, not on the basis of the experimenter's. Only a god capable of seeing a person's entire structure of inner goals could establish contingencies for that person without creating conflicts that would lead to a direct and violent confrontation. Even then, the god would be constrained to controlling the person in ways that created no uncorrectable errors in that person's control hierarchy.

Operant conditioning is only a modern term for what people have been trying to do to each other since civilization started. Everyone knows that people seek rewards and will change their behavior, within limits and as necessary, to get those rewards. But rewarding always implies withholding, and withholding what people need is a sure way to create violent and bloody conflict. An excellent case can be made for the statement that the present state of the world is the direct result of people trying to set up contingencies of reward for each other. It is time we realized that this principle of social interaction is the cause of, not the solution to, our most serious human problems.

Finally, I want to acknowledge the justice of some of the criticisms of my work. I know that I have overgeneralized in speaking of "behaviorists" when I really should have said, "some behaviorists." My aim is to find ways to effect a transition from what I believe is an outmoded view of the nature of human nature—and animal nature—to what seems a vastly more productive and humane point of view. My attitude toward what I see as the basic errors of behaviorism is not one of irritation or superiority. My model is only a feeble step in the right general direction. It is instead that there is an enormously difficult task ahead—but, considering what I see as the possible results of success, worth all the effort. I hope that Baum and Reese and other behaviorists will come to see it this way after careful consideration. I know their task is harder than mine, and it would be even harder if this clash of ideas were set up so that someone had to win, and someone had to lose.

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