ed that science and technology have now made it possible to obliterate mankind, and that these can be used for evil and destructive ends as well as for good and constructive purposes, the fact remains that while nearly all indices of the level of culture and civilization seem to have advanced not one whit in our century—and some of them seem to have retrogressed—in one field we can point indisputably to progress: in science and technology. If the history of science and technology can provide us with some hope for the future, if it can show us how man can transcend petty national rivalries and how the human mind can employ its reason for the solution of complex and disturbing problems which have long defied the human intellect and imagination—that is reason enough for turning to its study. This is not escapism from the realities of the present. Rather, by realistic appraisal of the road which man has trod in developing science and technology to their present eminence, we may gather faith and hope that the other problems which beset us may be conquered by the use of human reason, ingenuity, and imagination. And nowhere do these human traits show more clearly than in the study of the "newest" history: science and technology.

Experience and Experiment in Biology

Does blind probing threaten to displace experience in biological experimentation?

Paul Weiss

"Experiment versus Experience": if I had had to give this talk in French, I could not even have phrased the title as I did. For "expérience" in French stands for both experience and experiment. And yet there is a fundamental difference between the two. Experience means familiarity with happenings in the world. It is our cumulative record or store of judgments and suppositions, which we have formed by conscious or subconscious evaluation, from countless observations, impressions, and comparisons. It is personal and subjective. Experiments, by contrast, are objective tests of whether our suppositions are factually valid, not just intuitionally plausible or logically cogent. Experience makes us assume and expect relations between things in nature, but it remains for the experiment to verify the assumptions and expectations. Experience prompts and guides experiments, and the experiments in turn confirm or amplify or modify the content of experience. In short, experience, experiment, and logic play back and forth upon each other in mutual enhancement; it takes this triple interplay to promote knowledge.

However, in biology, the experiment has long been but a junior member in this partnership. It is fitting, therefore, to pay tribute to the period of Vallisneri, which we commemorate, for having raised experimentation to senior rank and status. It seems that during that epoch the number of converts from speculation to the discipline of the experimental method reached, in the terms of physics, the "critical mass" necessary to generate a carrier wave of telling force and sweep, whose mounting swell, washing away old rocks of idle supposition and contention, has brought on the stupendous growth of our understanding of living systems. So we may date from that period the systematic ascent of biological experimentation to its present culmination as the powerful tool for sorting fact from belief, for testing the pertinence of logical premises and conclusions, for settling ambiguous issues, for removing inconsistencies among conflicting data, and in general, for aiding the human mind in getting to understand living nature by manipulating natural events and tricking them into revealing crucial information.

The point is that experiments have been done, and ought to be done, for a purpose—a purpose other than just to do another experiment. Experimentation used to be deliberate, not improvised; planned to reduce confusion, not just to add profusion; it was meant to be relevant and incisive, not just trifling and redundant. Or, to put it succinctly, in the tradition of those past centuries, designing an experiment has been like training a gun at a target, rather than like spattering buckshot all around at random in the hope that somewhere something might be hit. The targets, in turn, were products of experience, including those extrapolations from experience by logic and imagination which generate hypotheses and theories. Throughout, deliberate orientation of experiments toward visible or envisioned goals has been the practice and tacitly accepted work rule.

Yet work rules have a way of changing imperceptibly as time goes on and as conditions change. Much as in evolution, such trends of change may be for the better or the worse, ending, respectively, in progress or disaster. But unlike evolution, intelligence ought to be able to recognize turns into disastrous courses in advance and thus prevent potentially monstrous products. For instance, let us take a complex system—an organism or a community or any social enterprise—whose proper functioning requires that all its vital parts maintain harmonious proportions; let one set of parts defy this harmony

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and go off on its own, with no regard to the others and the total pattern, and the result will be monstrosities. The dinosaurs, extravaganzas in size and mass beyond the power of a nervous system to manage and coordinate, were such monstrosities. Now, consider that the body of knowledge likewise is a cohesive, consistent, integrated system (*1*), not just a hodge-podge of miscellaneous information, which therefore likewise requires for its healthy growth a sound balance among its tributaries—experience, experiment, and logic. So, if biological research were to allow the share of experience to dwindle and let experimentation gain in volume, while losing in purpose and direction, biology might yet meet the fate of the dinosaurs. This is a fate which we can forestall if we heed signs, or even mere forebodings, that such a trend is in the offing.

Bulk Replaces Brains

Now, I submit that such warning signals have indeed appeared; that biological experimentation, at the height of success, is beginning to drift from the rigorous work maxim of its preceptors into habits that threaten to place bulk ahead of brains, and routine exercises ahead of thought. And since a historical occasion like this offers a welcome challenge to check our bearings for any aberrations from the charted course, I shall elaborate my reasons for this critical assertion.

I said experiments should be purposeful and meaningful. To be concrete, let me illustrate briefly some of those purposes and meanings. Organic nature confronts us with a host of puzzling questions, which we then try to answer by experiments. But the major class of experiments is that which boldly tosses questions back at nature and tricks nature into answering them by confronting her with combinations and constellations of conditions unprecedented in her standard repertory. To mention some examples at random: the taking of living cells out of the body and growing them in an extraneous medium—the ingenious experiment of Harrison that started tissue culture; or the surgical removal by Lashley of arbitrary fractions of the visual brain cortex in rats that had been trained to discriminate visual patterns, with the result that the learned patterns persisted in the defective brains as proof that visual memory is not a fractionable mosaic; or the first injection of foreign molecules into a rabbit, which then formed antibodies matching the alien agent, thus proving that immune responses are truly adaptive; or the transfer of the perfusion fluid of an excited frog heart into another heart, which thereby got excited, proving the humoral character of the transmission from nerve to muscle; and so forth.

What really distinguishes such experiments is not their novelty, but rather their originality and pertinence. Without imagination one can contrive infinite variations of experimental set-ups, all of them novel, yet utterly uninteresting, inconsequential, insignificant. The mere fact that something has not been done or tried before is not sufficient reason for doing or trying it. It takes originality to conceive innovations of true significance or of relevance to the solution of a problem or to the assessment of a theory. When Harrison removed nerve cells from the body to prove that they can sprout nerve fibers with no help from the body, he had expected the outcome. Experience had shaped his expectation, and the expectation dictated the experiment. When Lashley inflicted brain lesions in trained rats, his thinking was guided by clinical reports of functional integrity in human patients with brain injuries. The experiments were designed to settle problems. If they were gambles, the stakes were high. And incidentally, they all were done with rather elementary means—artfully. The crux is that they succeeded because these men had let their seasoned experience lead the way to critical experiments. This used to be the common practice. Is it still?

Accidental Discoveries

Or is my argument perhaps ill-founded? For instance, I have selected as examples star performers to the neglect of lesser lights. True, but stars of major brightness on the biological firmament used to be sufficiently distinctive to act as navigation guides for succeeding generations. The milky way is not well suited for this role. A crowd of mediocrity, however tolerable, if in the foreground, stands to becloud the guiding lights of excellence. There used to be, however, no such crowd. Next, I intimated that experiments used to be designed in expectation of a relevant result and that this was good. But is not scientific history full of instances of the accidental discovery of the unexpected? True again, but he who does expect something will be on the alert even for the unexpected, while he who just ambles, looking for nothing in particular, is prone to miss even the obvious. And as for the saying that the blind hen, too, finds a grain, this certainly would not hold for a hen on a grainless desert, and at any rate, it does not suggest that blindness or deliberate blindfolding is superior to vision. Of course, we frequently end up with answers to questions other than the ones we asked, or even with a lesson on how to phrase our questions better. But the historic successes of our predecessors still argue for the virtue of taking off for the exploration of the unknown from clearcut questions born from expectations, not just from vague expectancy of who knows what.

Experiments are also checks of whether what experience presents as obvious or plausible is true or false. The linkage of events in nature is a matter of experience; but to decide the nature of the linkage remains a matter of experimental tests. The remarkably observant Leonardo da Vinci noticed that castrated animals lose their fighting spirit, which led him to infer that there is a direct linkage between the testicles and behavior. It so happens that modern experiments have proved him right, but what if the behavorial change had been a by-product of the trauma of removing an organ—any organ—rather than specifically the testicles?

Plausibility alone is quite untrustworthy. Remember the case of the eruption of the fore limbs of the metamorphosing frog larva. These limbs develop inside a deep subcutaneous pocket; to become useful, they must break through the covering layer of skin, and indeed, when they have grown to size, perforations form in the skin, where the limbs chafe against it, letting the limbs emerge. What would be more plausible than to assume that the pressure of the limb itself causes the perforation? Distrusting plausibility, the skeptical biologist—in this case, Braus—put the assumption to an experimental test by suppressing the development of the fore limb altogether: surprisingly, at the appointed stage, an opening formed in the skin nevertheless, in readiness for the delivery of a limb, which was not there.

The puncture has since been traced to a coincidental autolytic process in the skin quite unrelated to the limb.

Biological research has uncovered a distressing multitude of such surprises. The question of why the eye lens is right where the eye is to look out seemed comfortably answered for a while when Lewis and Spemann both demonstrated in some amphibians that the lens would not form if the eye were absent, hence that the eye itself induced the lens. The comfort of this simple answer, however, did not last; for when the experiments were repeated in some other amphibian forms, the lens formed independently, whether or not the eye was there. Therefore, not only can sheer plausibility not be trusted, but, even if experimentally confirmed for one set of circumstances, the confirmation need not be valid for another set.

Another instance is chromatophore reactions: experimental studies on its control again brought widely disparate results, submitting to no unifying formula. In some forms, the control turned out to be neural, in others hormonal, and in still others, shared by both the nervous and the hormone systems, the one causing contraction, the other expansion. To come to this conclusion a fair variety of forms had to be sampled. Doubtless a more limited sample would have led to the false generalization that the control is either nervous or hormonal exclusively. To test a certain variety of species, thus, proved to have been an absolute necessity. Yet, once having established the salient point that evolution has made promiscuous use of all possible combinations between the agents and effects at its disposal, all further experimental repetition, except for training purposes, would only serve a cataloging function—expansion in bulk, rather than penetration in depth. But, we may ask, how large a catalog of data can we afford and justify?

Where Does Necessity End and Redundancy Start?

In fact, any set of examples of biological experiments that I could cite would make us ponder certain questions. What is the minimum range of variables that must be tested before we can certify a given biological proposition or conclusion as reasonably safe? How much additional variation and repetition beyond this range is essential and justifiable on scientific grounds, considering the finite bounds of social and economic reality? Where does necessity end and redundancy start?

In trying for answers, the biological sciences find themselves somewhere on middle ground between the one extreme of physics, which concentrates its interest on general principles, with less concern for specific mechanisms (except in meteorology and the like and, of course, engineering), and the other extreme of the historical branches of learning with their preoccupation with the particular, specific, and often unique shape of events. At the physical end of this scale, a maximum number of phenomena can be condensed into a minimum number of general formulas, but as one proceeds toward the other end, this ratio becomes progressively inverted, as itemized fact-finding and data-recording become more and more ends in themselves, rather than way stations to the formation of theories.

The center of gravity of the life sciences has steadily shifted on this scale from the descriptive and normative end of natural history toward the analytical and formulative end of the exact sciences. Of course, the assumption that biology could ever reach the physical end completely is a delusion, based either on lack of realistic acquaintance with living systems and their true nature or unawareness of the conceptual limitations of physical reductionism. This is not to question our success in reducing cellular phenomena to molecular terms. However, to pretend that the process can be reversed, that the molecular shambles can reassemble themselves into a functional living system without the cheating intervention of another living system is a conceptual perversion, whatever one may think of the primordial origin of life (*2*).

Biology therefore is destined to retain its autonomy, which means that to be known and understood, biological mechanisms will still have to be studied and formulated in their own right and full diversity. And this explains why in biology so many generalizations must stop far short of the vast inclusiveness of laws of physics, hence, why the range of validity of each must be determined empirically. It is this inherent feature of biological nature, rather than backwardness or extravagance, then, which necessitates testing over a far wider spectrum of variables, such as species, cell types, stages, environments, and so forth, than would seem necessary or even pardonable in most of physics. It sanctions the usage of repeating biological experiments with appropriate variations: with change of objects, agents, dosage, timing, methods of observation, measurement, recording, and the like. But when does usage turn into abuse? When is one to terminate potentially infinite series of variations? Or is it still legitimate, in the name of scientific freedom, to go on interminably?

This brings me to the crux of my argument. Throughout the phase of history which we have come to survey, till very recently, to be a scientist was a calling, not a job. Scientists were men of science, not just men in science. They had come to science driven by an inner urge, curiosity, a quest for knowledge, and they knew, or learned, what it was all about. They were not drawn or lured into science in masses by fascinating gadgets, public acclaim, manpower needs of industries and governments, or job security; nor did they just drift in for no good reason. The scene, however, is now changing rapidly. The popularity and needs of an expanding science bring in more drifters and followers than pioneers. While the first signs of this change are perhaps a little more conspicuous in our country, the growth of interest and investment in science, with mounting opportunities and recruitment, is bound to sweep across the globe. The carrier wave of experimental research set off in the days we celebrate is suddenly swelling into a gigantic tidal wave. Having barely begun, we cannot foretell its ultimate dimensions, but it is already bursting the narrow frame of current scientific facilities and practices, which have essentially been fashioned by and for traditional science, the small-scale enterprise of yesteryear. This growth will keep right on. Now, as biologists, we know that sheer expansive growth, unrestrained by differentiation and functional adjustments, breeds tumors. Shall we let the oncoming scientific expansion likewise become a tumorous inflation? Shall we let brainpower be overgrown by manpower and mechanical rote performance?

Growth in a healthy organism is self-limiting, restrained by inner balances, not by external strait jackets. In the growth of biological research, likewise, lest we conjure the horrible specter of some administrative authority prescribing to our scientists what to do, and what not, and how much, when and how, we must by all means strive to keep alive, or else revive, the old spirit of self-restraint of the experimenter, exercised by being most circumspect in the selection of his research targets in terms of relevance, and being most disciplined, responsible, and parsimonious in his attack on them. Research morality is even more important than research morale.

I had intended to cite specific evidence that as research has grown in volume it also has grown softer by loss of self-restraint, lowered selectivity, blurring of research targets, and, consequently, lack of self-direction. But then I decided not to quote because, after all, contemporary biology has such a superb record of truly outstanding achievements that it would gravely distort the total picture if only some flaws were drawn in magnified detail.

Nevertheless, the general conclusion stands: it is that however vigorously biological research has been growing, the diluent has begun to grow faster than the solid substance, and this bears watching. The symptoms are many. We see instruments turning from servants into tyrants, forcing the captive scientist to mass-produce and market senseless data beyond the point of conceivable usefulness—a modern version of the Sorcerer's Apprentice. We see bewildered youngsters composing research projects like abstract paintings: picking some colorful and fashionable words from recent literature, and then reshuffling and recombining them into another conglomerate, yielding a stew of data, both undigested and indigestible. We see narrow specialists lavishing their pet technique on reconfirming in yet another dozen ways what has already been superabundantly established to everybody's satisfaction. But why go on? Most of you will know the hallmarks of this growing dilution of our research effectiveness. They are irrelevance, triviality, redundancy, lack of perspective, and an unbounded flair for proliferation.

Now, granting the fact, why be alarmed? All right, there is some waste; but wastefulness can never be wholly banned from science. Yet, what is serious is that the volume production of trifles is not just waste. It actively competes with the pursuits of worthier objectives. The map of biological knowledge is still so full of major blanks and gaps that our elementary sense of proportions cries for an equitable distribution of our research potential over the whole field. Carl Hartmann (*3*) has recently published a list of major unsolved problems in the physiology of mammalian conception alone: it added up to 154, only a fraction of them under study. Imagine the size of such a catalog of ignorance for the whole of the life sciences. Yet dull, routine mass production in research only swells the traffic along the well-traveled familiar highways of activity, rather than branching out into the unfamiliar wilderness that needs to be explored.

Experience

These are just some of the symptoms of "Big Science." Well, Big Science is on the way and will remain here for good. The time to think how to adjust to it is now. This is a matter for all of those concerned with the future of our culture—research men, teachers, administrators, historians, philosophers, publishers, editors and statesmen. The growth of science can be the greatest blessing for humanity, but only if we resist the easy coasting downhill carried by the inflationary momentum. Ever more men of special technical competence will be needed in science to elaborate and apply that which we have come to know. They are not the ones I am concerned about. They are well taken care of. It is those others, able and destined to contribute significantly to the advance of knowledge, whom we must salvage from being either crushed or swept down with the current. They are those young men and women full of curiosity, imagination, and a sharp intellect, whose mental powers can find full realization only by exertion but would be doomed to atrophy in the dull and effortless game of routine mass procedures.

To them, the scientists of the future, we ought to pass on the lessons of our glimpses of the past. So, let me use—and, I hope, not abuse—today's festive occasion to bring to them some heartening advice on how to buck the tide: tell them to look at the old masters. Outmoded? Technically, of course; but not so much in method, and not at all in the spirit which guided their experiments. What were their guides? Ideas, not gadgets, not the need to publish. Ideas, in turn, sprout from the fertile soil of experience. So, then, at last, what is this potent nostrum, experience?

It is that subtly discriminating, screening, sorting, evaluating, and integrating faculty of our minds which we elaborate and perfect continuously throughout life, more subconsciously than in awareness. Its potency stems from the extraordinary innate acuity and sensitivity of our nervous system, sharpened and polished ever more by use and training. Our retina can perceive a few quanta of light, our nasal organ, molecules in concentrations below the detecting power of the finest tests. Why not concede, then, similarly high efficiency to the brain and give it free rein in its incessant activity of selecting, comparing, rating, judging, and creating, which is the mainspring of our concepts and ideas? The experimental discipline has rightly eradicated faith in any a priori truth of such ideas, but let us guard the young generation against seduction by the opposite extreme, no less pernicious: undisciplined experiments, unguided by ideas.

The principle that experience and experiment must be inseparably linked is universal and timeless. This fact gave me the courage to expound it before an audience from many lands and disciplines, at an event scanning the past for guidance to the future.

References and Notes

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