Government Policies and the Cost of Doing Research

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The political economy of science is a subject that did not need very much attention during the decades following World War II. We developed a wonderful system for doing science through a series of events mostly set into motion at the end of the war. At that time, vigorous public-sector support for fundamental research was guaranteed when a large military apparatus for research was converted, with remarkable suddenness, into one of the largest plowshares ever made.

Summary. The changes in the political economy of science are the natural outcome of two trends: science itself has become a more capital-intensive activity at the same time that federal support for research programs has slowed its growth. The results of the accumulating shortfall in the capital base for university research—increased seeking of support from private industry, efforts to circumvent peer review and competitive allocation, and a falling-out between institutions and investigators over how to divide up available resources—threaten to unravel what has been an extraordinary way of doing science.

Two important principles became attached to that great experiment. The first was the commitment to peer review as a method of determining what scientific programs should get public funding. The second was the decision that, for publicly supported fundamental research, the universities provided the best environment. The government could have taken quite a different course; it could have established a set of quasi-independent laboratories for which it sought cooperative support with the industrial sector, like the Max Planck Institutes in Germany; or it could have created a large array of government laboratories. That it did neither guaranteed that new discovery and the training of the next generation of discoverers would take place in the same locations, thus establishing one of the great strengths of American science. That strength is well recognized in Europe: at the 1977 Nobel awards, when Americans swept the prizes for the first time, our thoughtful Swedish colleague Suny Bergstrom pondered the phenomenon and finally attributed it to the "democracy of American science" (*1*). He meant the fellowship of the bench—the system of apprenticeship that is built upon the coexistence of research with research training.

The success of that experiment hardly needs elaboration here. Instead, I will concentrate on some strange symptoms that have been emerging in the past several years, and then make an effort to understand their etiology. Here are the symptoms.

- Georgetown University appeals to Congress for Department of Defense funding for a $160-million coal gasification fuel cell cogeneration program that will include construction of a power plant on the Georgetown campus. This is but one of several projects earmarked for specific universities that are taken directly to Congress, bypassing the competitive agency review process. The president of the Association of American Universities accuses Georgetown of "going by the law of the political jungle" (*2*).
- The National Institutes of Health (NIH) propose to withhold 10 percent of indirect cost reimbursement due the universities in the budget year 1983, citing recent increases in the proportion of indirect costs as a percent of total research costs. The House Appropriations Committee then adds report language to the NIH appropriation, increasing the total amount of NIH funding and instructing it to reimburse the full value of allowable indirect costs (*3*).
- The National Academy of Sciences Council passes a resolution noting that proper review systems "have contributed to the scientific preeminence of the United States," and urging "that the academic community and public officials exercise vigilance to protect this informed evaluation and decision-making process in the awarding of funds, not only for the support of scientific research proposals, but also for major scientific facilities and instrumentation" (*4*).
- The Federation of American Societies for Experimental Biology accuses university administrators of playing a "four-dimensional shell game" with indirect costs and describes them as having made a "triumphant tour de force in evading the issue in the past 3 years" (*5*).
- Hoechst AG and Massachusetts General Hospital sign an agreement whereby Hoechst supplies $67,300,000 for facilities construction and program costs for research on molecular biology (*6*).

What in the world is going on here? Can these things be related, and if so, to what underlying cause? Is our understanding of how to do science coming apart? Has the glue vanished from our traditional concept of what is the responsibility of industry, of government, and of the universities?

I do not think so. But I do think that our kind of science is crossing a significant watershed. It is hard to know exactly where to locate the divide, but the terrain contains an important transition from people to property, and from operating to capital budgets—at which point we must start worrying more about one-time equipment costs and facilities renewal than we do about salaries. On the maps, the territory on the other side of the divide is labeled Big Science.

The Advent of Big Science

Over the past decade, a number of disciplines have crossed over: organic chemistry, various parts of solid-state physics, and molecular biology. The rest of cell and developmental biology is well on its way. In the 1960's, the main problem for department heads in making appointments had to do with billets: that is, with persuading the dean and the provost that the growth potential of our discipline justified the retention of an additional faculty position. A decade later, an interesting transition occurred. Although we still worried about billets, the

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main problem became whether we could commit the equipment and space renovations necessary for the new appointee to do the work. The capital cost of the equipment and special facilities, in short, had become larger than the capital value of the endowment necessary to yield the faculty member's salary. That is as good a definition as any of Big Science. It immediately raises the most serious questions of resource allocation—for example, do we need to consider new patterns of sharing, even between different institutions? Thus we now find ourselves engaged with the very questions that have preoccupied high energy physics since the 1950's.

That would not be very difficult for the scientific enterprise if we still faced the same economy and the same policies that obtained when we began our exploration of this new territory. Through most of the 1960's, federal support of basic science was adequate to handle both the operating-budget side and the modest capital demands associated with most scientific work. Toward the end of the 1960's, two things happened. First, we witnessed the end of federal support for the construction of research facilities. Second, with respect to equipment, the situation has been even worse. The rising demand for more and more sophisticated instrumentation has confronted a declining federal commitment to pay for expensive capital equipment. The expanding consequent shortfall has been documented in the 1980 instrumentation survey conducted by the Association of American Universities for the National Science Foundation (*7*).

That survey served as the basis for a request in 1980 by the Carter Administration for a special $150-million appropriation to the National Science Foundation for research equipment, which would have been a down payment on a total liability that was estimated to be $1 billion (*8*). The item was stricken in the revised budget request by the Reagan Administration, and no adequate effort to deal with the problem has been mounted in the intervening 4 years. In fiscal year 1984 the total federal investment in R&D plant in universities is projected at $40 million (*9*). Thus, although there has been modest real growth in federal operating budgets for research and development during the past few years, the capital gap has been widening for much longer than that.

There is something very predictable, indeed almost implacable, about the behavior of an unfunded liability—and science is a vigorous and thoughtful activity that instinctively senses its own needs very well. Therefore, I argue that the political spasms that we are now seeing result from the struggles of the scientific venture to escape the prison of its own undercapitalization.

Politics and Scarcity

Before discussing the events themselves, let me briefly sketch the motivations and the behavior of the different players: Executive government, Congress, the universities, and the scientists themselves. All are in agreement on some basics: the importance of science, the essential desirability of seeing it supported effectively, and the need to divert resources to the best work. But each group has particular responsibilities, needs, and political roles—so the behaviors differ.

Executive government is accountable, eventually to the voters, for effective programs. Most government agency budgets distinguish poorly between one-time capital expenditures and "budget-base" monies; there is thus an unhealthy incentive to avoid the former in order to make one's own annual budget request look better and support the kind of fiscal responsibility to which American voters are increasingly sensitive. To such agencies, and to Congress as well, scientists are an important constituency, and university administrations much less so. The rules for this are fairly simple. First, more abundant economic units usually have greater weight in the political process; that is why associations of automobile dealers wield more influence than associations of automobile manufacturers. Second, working scientists are much more fully and effectively integrated into administrative and policy processes in the research agencies. Yet, despite their relative lack of influence, it is the universities rather than today's scientists that have the greater long-term interest in the quality of capital facilities as opposed to operating expenses.

That, then, is the background: a capital deprivation of some 16 years' duration, begun at about the same time that federal support for research programs slowed its growth and fell onto an uneasy, variable plateau. And in the meantime, the scale and the obligations of the scientific venture continued to grow. We now find ourselves caught in a mismatch between the needs and expectations of scientific research, on the one hand, and the willingness and capacity of the public sector to support it, on the other.

The results are predictable. Whenever resources are scarce, their allocation becomes a matter of desperate controversy, and alternatives previously unconsidered begin to claim attention.

The symptoms that I highlighted above and that have captured the attention of the media reflect three manifestations of the current crunch. The first is an increased attentiveness, on the part of the universities and investigators alike, to private sources of funds as a substitute for federal ones. The second is a disturbing incipient collapse of the agreement between the performers and sponsors of research, that peer review is the fairest and most effective way of awarding scarce resources. The third—and it is the most distressing of all—is a falling-out between the proprietors and the doers of scientific work over how the research venture is to be supported.

Private Funding for Research

The interest in private sources of funds strikes me as more reassuring than troubling. It was inevitable that universities would turn more to commercial sources of support as government began to flag; and it is equally inevitable that proprietary organizations would, in the new style of venture capital, begin to try to assert possession of ideas at an earlier time in their evolutionary history. That has meant a refocusing of commercial interest upon more basic, as opposed to merely applied, research, and this, in turn, has produced some problems.

The most serious involve the division of energy and effort of faculty members between their own university laboratories and small proprietary ventures in which they have an equity interest. Significant disputes over intellectual property and substantive conflicts of interest with respect to the independence and well-being of graduate students and fellows have both emerged. One can only hope that most of them have been fairly resolved, but we are gaining a grip on the problems, and a sensible pattern of accountability should eventually emerge.

In general, the larger scale arrangements between universities and industry consortiums or major single firms have offered far fewer difficulties. Over the years, the universities' standards for crafting such broad, formal agreements have been pretty thoroughly tested by government, and thus most of the prospective problems have been solved in advance. Just in case universities were tempted to forget those principles, the government gave them a sharp reminder on openness of research just as many of the new industry agreements were coming along. Efforts to apply arms export control regulations to fundamental research reminded us that freedom of exchange and openness of publication are important attributes of fundamental science. Admiral Bobby Inman's warning that the universities should not keep secrets for profit that they would not keep for patriotism was probably unnecessary: but it did usefully emphasize the point, and at just the right time (*10*).

Despite the public fuss about increased industry sponsorship of basic research, something less than 5 percent of university research is actually now supported by industry, and that fraction is growing only imperceptibly. The appearance of a few special arrangements in areas of particular commercial interest is not a harbinger of wholesale substitution of private for public dollars in the support of fundamental research. Indeed, a drop of 1 percent in the federal support of university science requires a 20 percent increase in industry support to make up for it—distinctly unfavorable leverage. A general private rescue from public obligation is clearly not in sight.

Peer Review

The second phenomenon—the incipient dismantling of part of the peer review system—is more surprising. It has always been true that occasionally a university or a state has been awarded a particular research facility by a friendly congressman; and of course a special kind of regional allocation has always been present in the agricultural sector. Recently we have witnessed an unparalleled spasm of noncompetitive set-asides for special facilities in particular places. They involve not just the Georgetown case (now not included in the Department of Energy request for 1985), but also such diverse institutions as the University of Oregon Health Sciences Center, Catholic University, Florida State University, and Columbia University (*2*). In fact, Columbia and Catholic probably started the present round 2 years ago, by engaging a Washington lobbying firm to intervene on their behalf in adding special facilities for chemistry and vitreous-state materials, respectively, to the Department of Energy budget (*2*). They were successful, and that has led others to try as well. The growing epidemic is the more surprising because of the unanimous approbation that we thought adhered to the processes of peer review and competitive allocation. It is as though three or four civilized nations had decided, all at once, to return to whaling.

A dangerous prospect, of course, is that each defection increases the sense, on the part of those who retain commitment to the consensus, that there will soon be nothing left. (In that respect, too, one is reminded of the international control of whaling.) Although the Association of American Universities and the National Academy of Sciences have both deplored these departures from the convention (*11*), the smell of pork, or is it whale meat, may prove too tempting. The optimists are hoping the problem goes away and the pessimists are getting to know their congressional representatives.

Indirect Costs of Research

The last of the three embodiments of scarcity is, as I have said, the most troubling. It has already had harsh political ramifications, ones that have been felt on the campuses as well as in Washington. It is especially deplorable because it pits friend against friend, and threatens to unravel the basic fabric of understanding and trust that has supported our science for 30 years. I am referring, of course, to indirect costs.

The fraction of total research costs that go to pay indirect costs, or overhead, has increased steadily over the past decade. The increase has been quite modest for some government agencies—National Science Foundation, for example; but it has been steeper in others, like NIH.

For years, government policy has held indirect costs to be an entirely legitimate part of total research costs. These costs cannot be allocated easily to particular projects: they include the operation and maintenance of buildings; departmental, general, and research grant administration; depreciation or use charges on facilities and equipment; student services; and libraries. They are calculated according to an often-reviewed system developed by the Office of Management and Budget and set out in OMB Circular A-21 (*12*). Basically, the rules require that cost pools be created for each category; the proportions of total costs in each category attributable to instruction and to research are then calculated. The ratios are used to ensure that indirect costs are charged to the government only when they are associated with research-related activities or other sponsored agreements. Thus, for example, only those costs of the library associated with organized research are spread over government-sponsored research projects and only the consumption of heat and power associated with research activities can be charged to government-sponsored research. The total of such indirect costs allocated to research is then divided by the total of modified direct research costs to yield the rate. The formulas have been revised repeatedly and reviewed by independent accounting firms (*13*). The details may perhaps stir disagreement, but I think most would probably conclude that the rules are fair.

How, then, can the proportion of indirect costs as a fraction of all research costs be increasing? There are several reasons.

1) Inflation affects some cost items, (such as energy), much more than others. To the extent that these items are research-intensive and are paid through the indirect rather than the direct route, there will be a disproportionate increase in indirect costs.

2) Cost-accounting studies done by universities on research have been steadily refined and improved, largely at the urging of the government. Increasingly, therefore, they have identified and captured costs to which the universities have always been legally entitled. In the early days of indirect costs, everyone was underrecovering. Many state universities still are because in these institutions reimbursement flows to the state treasury, and the universities lack the incentive to expend resources on the documentation needed for full recovery. A corollary is that indirect costs vary widely among different kinds of institutions. This variance does not indicate that the whole thing is irrational; on the contrary, it is yet another instance of the rational power of economic incentive (*14*).

3) Changes in research volume and the adequacy of direct support put additional pressures on indirect costs. Reductions in the rate of growth of government funding have caused a saturation of research volume in many institutions. Those indirect costs that are fixed must then be spread over a relatively smaller number of direct-cost dollars, and the rate rises. In addition, NIH in particular has recently pursued a strategy of underfunding in order to maximize the number of grants it can award. Investigators, universities, and Congress have tried to discourage this practice. This year, in spite of the substantial NIH budget restorations and in spite of explicit Appropriations Committee language, one institute made across-the-board cuts in all grants (*15*). Since a large proportion of indirect costs are fixed, underfunding of

the direct costs will cause the proportion of indirect costs to rise. These effects of volume are often magnified by the government's rules about reimbursement. The difference between the negotiated rate and the actual rate appears after the fact; when unexpectedly low volume, for example, produces an actual rate that is higher than expected, the difference may be collected by an increase in the rate for succeeding years. On this basis, many research universities have accumulated large carry-forward costs during the present period of volume saturation, and this provides an advancing wave of upward pressure on the indirect cost rate.

4) Over half of the indirect costs of research are associated with facilities, and among those one of the significant contributing costs is depreciation or use allowance on capital equipment and buildings. These cannot be recovered by universities, of course, if the government has financed the building or purchased the equipment; that would be collecting twice. As long as the government was financing most of the buildings and essentially all the equipment, this was a minor element in recovery. During the 1970's, however, the government essentially stopped supporting construction of research facilities. At the same time, it became increasingly common for major pieces of equipment to be supplied to the institution from private sources, and this trend accelerated as the tax laws were changed to give more favorable treatment to equipment donations by manufacturers. For example, between 1968—the last year of the Health Research Facilities Act—and 1983 Stanford's indirect cost recovery rate practically doubled. The annualized growth rate for sponsored research over that period was about 6.5 percent. For the administrative components of indirect costs, it was about 9.5 percent. But for the depreciation and use charges, it was 11.5 percent.

Indeed, an examination of the inflation rates for various categories of indirect cost over the past decade bears out the extraordinary significance of facilities—and the relatively lower impact of those administrative categories so frequently blamed for the effect. The annualized rate of inflation of modified total direct research costs at Stanford was 1.18 percent higher than the Bay Area consumer price index for the period 1974 through 1983. Reflecting their general relative increase, indirect costs grew at 4.34 percent on the same basis over the same period. But if the indirect costs are broken down into their component pools, the aggregate of building-related costs (operations and maintenance, equipment, depreciation, and use charges) is revealed to have an annualized growth rate of 8.41 percent, whereas administrative costs (general, departmental, sponsored projects, and student services) have grown at only 0.30 percent per year (*16*).

Despite these straightforward explanations for the phenomenon of increased indirect costs, NIH has, for two consecutive years, attempted to withhold 10 percent of already-incurred indirect cost recovery from the universities, but so far Congress has denied that effort.

The worst thing about the NIH strategy is not that it would have depleted the general funds of the universities, although that is true, but that it has produced extraordinary divisions between principal investigators and university administrators. The administrators do, after all, have an obligation to preserve both the operating and the capital prospects for original scholarship, as well as to make sure that the general fund is healthy enough to support salary improvement and other worthy purposes. For a private research university like Stanford, indirect cost recovery from the government is characteristically the second most important income source, behind tuition but well ahead of all endowment income. If it shrinks, then either something else on the income side has to swell (and almost nothing can), or something on the expenditure side has to shrink; it is that simple. Thus, it ought to be in any faculty member's best interest to support fair reimbursement for indirect costs. To date, administrators have not done a very good job, either of persuading faculty that some of the functions supported by indirect costs are well run or explaining the economics and the policy that underlie indirect cost recovery. In consequence, when NIH proposes to principal investigators to increase the number of grants at the expense of indirect cost recovery to the university, it sounds like a bargain, even though it is anything but.

It is not surprising that the indirect cost matter has stirred controversy between scientists and their university administrations. Some principal investigators took the position that more money could be put into their own research activities if the universities' reimbursement was cut. Others, who saw the relation between legitimate recovery and the payment of such expenses as faculty salaries, were not so enchanted. But nearly all were troubled.

Like many controversies, however, this one has had some unexpected and salutary outcomes. An informed coalition of university associations and scientific groups helped in obtaining full funding for both direct and indirect costs in this year's budget. That coalition accomplished the replacement of the $75 million in indirect costs that NIH had attempted to withhold, and also restored about $140 million in direct costs. From the success, we learned that squabbling over categories of research costs is not only divisive, but self-defeating. The Federation of American Societies for Experimental Biology has also reversed its position on indirect costs and passed a resolution calling for cooperation between university administrators and bench scientists.

It is not, however, part of the bargain for the universities stubbornly to insist that all is right with the indirect cost picture. The problem needs a broad reexamination on a government-wide basis, led out of the Office of Science and Technology Policy. The result of such a study, which is under way now and in which university associations and scientific organizations are both participating, may well be some limitations upon one or more categories of indirect costs. That may be acceptable, especially if there is some trade-off relief from accountability documentation or other administrative requirements that would give universities real cost reductions and not just loss of recovery. What is not acceptable is an arbitrary action by one piece of the government that attempts to divide the academic community.

Conclusion

I have tried to suggest that the sea change in science policy, evidence of which is all around us, is a natural outcome of two evolutionary trends. The first is of our science itself, to a more and more capital-intensive activity. The second is an accumulating shortfall in the capital base for university science, resulting from a failure of the public patrons of science to acknowledge the importance of that kind of investment. That shortfall has produced, or at least exacerbated, a number of events: increased seeking for private industry support by universities; heavier temptations to circumvent the ordinary processes of peer review and competitive allocation; and squabbles over how to divide up, between institutions and investigators, the pool of resources available to support scientific work. Indeed, the indirect cost problem itself is in part a consequence of chronic undercapitalization.

The squabbles and the policy challenges will be more easily resolved if we understand their origin. In addition, we must focus our attention on the problem of institutional capacity and the health of capital resources. In comparison with what is available elsewhere, and what ought to be available to us, our environments are significantly worse then they were a quarter century ago. We owe to the next generation of students and faculty members an opportunity to do science as close to the forefront as all of us have been able to do it. Commitments only to the number of research grants next year, or to the total programmatic support of research in the federal budget, will not make that happen. It will only perpetuate the present liability, extend the divisions between researchers and institutions, and blunt the promise that our extraordinary way of doing science has created.

References and Notes

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3. House Committee on Appropriations, *Department of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Bill, 1983*, 97th Cong., 2nd sess., 29 September 1982, H. Rep. 894, p. 26.
4. "Statement of the Council on Federal Funding for Research Facilities and Instrumentation" (National Academy of Sciences, Washington, D.C., 30 October 1983).
5. *Fed. Am. Soc. Exp. Biol. Newsl.* **16**, 2 (March 1983).
6. Agreement between the General Hospital Corporations and Hoechst AG, 13 May 1981.
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8. The Carter Administration responded by requesting, as part of its fiscal year 1982 budget request, an additional $75-million appropriation to NSF for research equipment. This funding would have been only a small "down payment" on total liability estimated at over $1 billion ["Special analyses, budget of the United States Government, fiscal year 1982" (Office of Management and Budget, Washington, D.C., 1982), p. 314].
9. "Federal funds for research and development, fiscal years 1982, 1983, 1984" (NSF 83-319, Division of Science Resource Studies, National Science Foundation, Washington, D.C., 1983), vol. 32, p. 121.
10. B. R. Inman, *Aviat. Week Space Technol.* **116**, 10 (8 February 1982).
11. B. Schorr, "Breaking tradition, more colleges go directly to Congress for funds," *Wall Street Journal*, 5 March 1984, p. 29.
12. For a review of the rules and requirements of recovery of indirect costs, see Ad Hoc Committee on Government University Relationships in Support of Science, "Strengthening the government-university partnership in science" (National Academy Press, Washington, D.C., 1983), chapter 6, pp. 117–145.
13. The most recent such review was conducted by the San Francisco accounting firm of Peat, Marwick, and Mitchell in 1977.
14. As would be expected, the variance is markedly reduced when only similar institutions are considered. In addition to the important distinction between public and private, there are expected differences in rate between medical schools and other research areas, and between large- and small-volume performers. If one considers only those research universities that are (i) private, (ii) have medical schools and include them in the rate, and (iii) have large research contributions from both medical and nonmedical components, the following indirect cost rates may be compared for fiscal year 1984: University of Chicago, 69.0; Columbia University, 69.7; University of Pennsylvania, 65.0; Stanford University, 69.0; and Yale University, 68.0.
15. The underfunding strategy is disclosed in a letter from W. F. Raub, deputy director for extramural research and training at the National Institutes of Health, to A. Merritt, director of the Office of Research Administration at the University of Pennsylvania, in February 1984. Raub states, "While most Institutes are making only 1 to 2 percent reductions, the National Institute for Arthritis, Diabetes, and Digestive and Kidney Disease has found it necessary to make a larger reduction to fund its proportion of the approximately 5000 grants that the National Institutes of Health will be awarding in FY 1985."
16. These growth rate measurements were made from audited Stanford data on the actual indirect cost pools. Similar figures for the cost allocations would differ less, because in the process of arriving at the latter, each cost category is subject to proportional cross-allocations from the others. Thus, for example, general administration receives a cross-allocation from the operations and maintenance pool, so that it will include the costs of maintaining and heating space used for that activity. The effect of this cross-allocation will be to "load" the purely administrative costs with the more rapidly inflating building-related costs. The indirect cost pools themselves are uncontaminated by this effect.

RESEARCH ARTICLE

Nucleotide Sequence and Expression of an AIDS-Associated Retrovirus (ARV-2)

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A wide variety of diseases in many animal species are a consequence of infection by retroviruses (*1*). A distinct group of human retroviruses has been isolated from patients with the acquired immune deficiency syndrome (AIDS) and individuals with related conditions, such as persistent lymphadenopathy. Several independent isolates, called lymphadenopathy-associated virus or LAV (*2*), human T-cell lymphotropic virus type III or HTLV-III (*3*), and AIDS-associated retrovirus or ARV (*4*) by the laboratories of origin, are similar with respect to morphology, cytopathology, requirements for optimum reverse transcriptase activity, at least some antigenic properties, and some restriction endonuclease cleavage sites in viral DNA. Epidemiological studies show that infection by one of these viruses may be a necessary condition for the development of AIDS, although predisposing factors may contribute to the onset of the disease (*3–10*).

Molecular clones of HTLV-III, LAV, and ARV-2 have been described (*11, 12*). These clones provide material for analyses of viral structure, viral replication, and mechanisms of pathogenesis as well as for measurements of similarities and differences among the retroviruses associated with AIDS and with other retroviruses. In this report, the genetic structure of an ARV isolate is established from the sequences of molecular clones of ARV-2 DNA (*12*) and from the partial sequence of virion proteins.

The DNA sequence of ARV-2. Proviral DNA and circular unintegrated viral DNA species from ARV-2 infected cells have been cloned in bacteriophage λ (*12*), and the structures of five recombinant phage containing ARV-2 DNA were characterized (Fig. 1). The nucleotide sequence of various regions of each of these molecular clones was determined and used to establish the complete sequence of ARV-2 DNA. The sequence variations in ARV-2 DNA in these phage are presented in Table 1.

Long terminal repeat regions (LTR's). The LTR's of retroviruses participate in the integration of the virus with the host cell and in the regulation of transcription of viral genes (*13–15*). To define the

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