

special feature/a conversation about our recombinant future



Biotechnology in 2018: How will genetic science and technology change the world?

ROBERT BAZELL: It used to be that scientists practiced their craft in universities or in big drug companies and didn't talk to each other too much. When the technology of recombinant DNA came along in the early '70s, it occurred to a few very bright people that

The potential: In dreams
begin responsibilities



biology suddenly wasn't just a descriptive science any more; it had the potential to make products, and make products very quickly. And so they started these things called biotechnology companies, and one in particular, [Genentech](#), on the day of its initial public offering in 1980, went from an opening bid of \$35 to top out at \$85 in a matter of a few hours. Nowadays you get that kind of action on Wall Street with chicken companies, but in those days that was an unusual Wall Street event, and it got the attention of a lot of people who knew nothing about biology (let alone biotechnology) to pay attention. Biotechnology started to become synonymous over the years with very high risk and high reward.



Harry Griffin, Robert Pollack, Robert Bazell, Barry Bloom

I have heard from friends who work on Wall Street that the biotechnology companies that are doing the best right now are not companies that have products (which are an extraordinary minority anyway); they are companies that have stories. They come in and tell investment bankers the story: that they are going to find a cure for arthritis, to completely make arthritis go away; they know how to do it, and they have the top scientists, and it's going to happen. Those stocks are doing better than the companies that have products, because if you have products you can test them and find out whether they work in a finite period. But biotechnology is an interesting thing: It's changed the landscape of how biology functions [in universities](#) and in the relationship between pharmaceutical industries. So I think we want to start out by asking, What is biotechnology capable of achieving? Is biotechnology going to do anything different for us, with all its investments and capital coming in, from what would have happened if there weren't this industry?

HARRY GRIFFIN: I certainly think that biotechnology has the potential for this. What we've been doing in the past a lot of the time is descriptive biology. It's using the genetic variations that exist around us. But in the future--already--we can create our own genetic

variations. In the field that our institute is in, we're introducing human genes into cattle and sheep to produce therapeutic proteins in their milk. The creation of material by genetic engineering wouldn't happen without biotechnology, without the revolution in understanding molecular biology and the structure of DNA. So I think that the potential is there for something quite different than we have had in the past.

BAZELL: Barry, from where you sit, is biotechnology changing the world?

BARRY BLOOM: Not yet, but I think the word that you will hear an awful lot here is *potential*. Biotechnology is the application of science to dreams--and not everybody in the past in science has dreamt either very deeply or far, or in a practical way. [Robert Oppenheimer](#), one of the people who made the first atom bomb, said that the deep and profound truths in science were arrived at not because they were important, but because it was possible to find them. [What makes it] possible to find them is the technology and the harnessing of imagination. I think the potential to harness the imagination and reduce it to products is a marriage that has been very inefficient. One group of people look for knowledge; another group of people in companies look for products. It was a very slow process, trying to link the two. This happens on an hourly basis in biotechnology.

BOB POLLACK: I appreciate that Barry Bloom has referred to a great, now dead physicist for a reference on biotechnology, and I'd like to do the same. A colleague of mine, now recently dead, Robert Serber, was No. 2 to Oppenheimer in the theoretical section of Los Alamos in the development of the atom bomb. And Serber after the war was one of the founding organizers of [Brookhaven National Laboratory](#) on

Long Island. This laboratory is a marker of America's late-stage potential loss of leadership in high-energy physics, as its big cyclotron looks never to be built, but when Serber was building Brookhaven in the '50s, he says in his



[autobiography](#), he noticed that the time it took to get out to Brookhaven was constant even as the technology of getting there kept changing for the better. When he began, he had to drive out on back roads. Then the Long Island Expressway opened, and then the Long Island Railroad changed its stations, but getting to Brookhaven always took an hour and a half over a 30-year period.

I want to use that story as an excuse not to answer Bob Bazell's question. That is, I don't think we know--and I don't think it's wise to speculate linearly from what we know--what the technology will look like in 20 or 30 years. I'd rather answer the question to say what it will feel like to be inside of whatever technology is likely to come, rather than speculate on how many new products there will be or what they will look like. My strong sense is that the change in our lives which will come from this technology will be sensed as a loss of what we now think of as our freedom to change ourselves. It will be, unless we're careful about it, a setting in of a kind of DNA-driven determinism, where what you are born with in each of your cells, as your particular unique version of the human genome, becomes more and more a statement of your future as well as your ancestry. By 30 years, there is a chance that we will measure our age by how many years we have left rather than by how many years we have been alive. That will be a major political change in all societies, no matter what their other political structures are. You can imagine people who have five

years to live being a constituency with some force, even if some of those are the parents of kids with inborn genetic disease, and some are people who are very old and now have a diagnosis but not a cure. I think this technology drives diagnosis without cure, and we are not as a society well prepared to deal with the consequences.

BAZELL: That's an interesting and very sad extrapolation of the current ability to determine diagnosis without cure, without thinking that that problem in itself can be solved.

POLLACK: I don't know when the cures will follow from the diagnostic technology, nor do I know that they won't. But I'm saying, as both my colleagues have said, we're in a window now where the technology of determination of what's in your DNA is very fast-moving. Many of the dreams that Barry refers to are dreams of the utilization of individual diagnostic differences in inherited DNA. There are many marketable tests for whether you have inherited a propensity for a future problem. My sense is that right now we have opened up, in our field as scientists, an ethical obligation to follow those determinations as quickly as possible with something to do about them. And I don't see a similar market-driven obligation to do something about the tests once the test is available. I don't know that that wouldn't change tomorrow, but as of today that's the way it looks.

BAZELL: Harry, do you share that grim outlook?

GRIFFIN: I don't. I think that's a rather pessimistic view in that I think it's elevating genes to a major part of our future. There are obviously some cases where our genetic makeup has got some pretty obvious consequences: One in 25 of us, or at least those of us who are Caucasians, carry the [cystic fibrosis gene](#), and at present the life expectancy of someone with cystic fibrosis is not much more than the late 20s or early 30s; but that's a condition that's been known for some time, and treatments are being developed. I think when it comes to other genetic propensities, we're into areas of risk, and I think risk is something that society, both collectively and as individuals, finds exceedingly difficult to handle. If you were told, for example, you had a 50 percent chance of breast cancer, but the only solution was radical mastectomy, what sort of choice is that? On the other hand, if you were told you had a 10 percent risk of serious illness, would you do anything about it? People in general tend to ignore risks; at least those of us who smoke ignore risks. I think information presented in this way is going to be very difficult for individuals to handle.

BAZELL: But a lot of people would say that the cloners of [Dolly](#), which raised all this ethical issue about an identical genetic copy of something, would have a strong interest in saying the genes aren't all that important. Suddenly we're back to nurture, because we can just reproduce the genome like a rubber stamp.

GRIFFIN: Well, we have human clones already, and we have studied them extensively. Anybody who is an identical twin is genetically identical, and we know that genetically identical twins grow up to be different. We know roughly how different they are if they are raised in a similar environment. There are certainly different personalities in individuals and to suggest that they are not as human as the rest of us is clearly not true. Also, if they have a genetic predisposition, both of them, if they are identical twins, would have that predisposition. But we've lived with that type of issue for some time.

BAZELL: Well, let me ask Barry a question about the cloning, because you [Dr. Griffin] have obviously spent a lot of time

The economic motives: will markets



talking about Dolly. These people did something that had astounding implications for society, at least theoretically, and yet they did it for a very small reason. It wasn't this monumental [effort] to find out whether they could clone an adult mammalian cell; they wanted to find a more efficient way of mass-producing proteins. Is that kind of market-driven force going to become more common with biotechnology? Is that a risk of biotechnology?

BLOOM: I don't see that as a terrific risk, because I think that is how science is done. Biotechnology derived from a set of experiments done by [Joshua Lederberg](#), who had won the Nobel Prize for genetics, and he was not inventing biotechnology. He had no interest at that time in inventing genetic engineering. As I like to say, he was interested in [sex in bacteria](#): Do they have it or not? The profundity that came out of that is that required not evolution by one mutation at a time but by recombination of big pieces of DNA from one bug to another. And once that experiment was done, it was not, as I understand it, his vision that this would give rise to great new industries upon which we could levy taxes. But in fact it was the pursuit of science. Monoclonal antibodies came out of a very different kind of fundamental inquiry. Cancer cells didn't do things specific for tissues from which they derived; they de-differentiated. Antibody cells were not immortal. What would happen if you stuck the two together? Could you get a cancer cell to carry out a differentiated function like making antibodies continuously? That was the question that [Cesar Milstein](#) asked, and what came out of that was monoclonal antibodies.



BAZELL: But are people asking those questions nowadays not because of an intellectual curiosity, but because they are thinking about what the investment bankers will fund them to do?

POLLACK: I think it is an unnecessary diversion to worry about the market. The question is not whether people are motivated to become wealthy; it's terrific to become wealthy. The question is whether what motivates them to become wealthy converts into something actually useful. Scientists are protected from the obligation to become wealthy, if they don't choose to, by peer-reviewed, federally mandated large sums of money for basic research, which keeps us a leader in world basic science. I think that will go on, independent of the question of the technology that comes from it. But, as this is a biotechnology panel, Josh Lederberg's motivations are not relevant to the questions you've asked. The questions are, Once basic science produces an understanding of nature which generates the possibility of marketable material, will the market then produce something of benefit to the population of the people who can buy it, the people who can't buy it, the people who don't know about it, and the rest of the species as a species?

On this planet most people still die of infectious diseases, not of inherited differences, and most people still could extend their life by 19th century public health changes, not by what I would call boutique medical improvements driven by DNA data. Nevertheless, this 7-8,000 Standard & Poor stock market is not interested, by and large, in matters that people can't pay for, and most of the people who die young can't buy the kind of materials that would keep them alive if the technology were producing them. So I think there's a poor match of what the species needs and what the market wants. That is an issue not for basic science but for biotechnology. Large companies tithe some fraction of their profit to

Third World matters; the [Wellcome Trust](#) is a huge gift to basic science from profit; so is the [Hughes](#) foundation, when you go back to its origins; but the market itself is not a charity. The market itself is out to make a profit. Your question, I think, is, Can one benefit from profit, in a medical sense or in a social sense? I'd say it's a mixed answer. We don't know, but we're not assured of it. And we have some obligation in the technology to do more than wait for the market, but in fact I would say, in intellectual terms, regulate the market to be sure we at least don't make matters worse for the species in the business of making money.

Let me give an example of making matters worse. If you genetically engineer a plant so that it is resistant to an [insecticide](#), so that you can put more of your insecticide in the soil and still get your crop out, it seems to me that's a short-sighted way to have a profit-making product. There are large biotechnology companies which make genetically engineered food plants whose genetic engineering is not to improve the yield directly, but rather to allow larger doses of insecticide and pesticide and herbicides. That seems to me a bad technology on the face of it.

BAZELL: Let me rephrase the question. Is the structure of funding that is now provided by biotechnology changing the kind of questions that are being asked? Is there enough money and enough motivation for the Joshua Lederbergs and the Cesar Milsteins to ask the kind of fundamental science questions that led to all that change, or are we moving to an environment where we only ask questions that somebody who isn't a scientist can see as having at least the potential for a profit?

GRIFFIN: I don't think we are moving to that situation. In the U.K. we are often criticized for doing excellent basic science but not converting that into practice, and there's clearly got to be a balance. If you move too far towards practical applications, then the ideas will tend to dry up from the basic science. It's a matter of trying to get the balance correct. As far as the issues with the Third World go, I'm not sure that we're justified in selecting biotechnology as a particular focus here. We all consume more than our fair share of resources in Western Europe and in the U.S., including something so basic as food and fuel. I don't see why you should particularly select the biotechnology industry out for criticism or for focus in this regard.

BAZELL: Shouldn't we look at precisely why we are here? Because, as Barry said, it's hope; it's something different. Do we have the right to expect it to be better in any way than, say, the steel industry or the oil industry?

The historical context: Global equalizers vs. boutique treatments



BLOOM: It would seem to me that there is a continuity in science. Even if it's not all good. A profound testimony to science is reflected in a graph¹ put out by the [World Bank](#) from the best demographic data available in the world, by the dean of arts and sciences at the University of Pennsylvania, [Sam Preston](#). It addresses the following question: Is there a relationship between per capita income and life expectancy? It doesn't sound like a scientific question, but if you'll bear with it, I think it has a profound application to one's thinking about science. There's a set of four sweeping curves for 1990, 1960, 1930, and



1900. In life expectancy, if you took per capita income normalized to 1991 dollars, what you would find is that people with as little as \$4,000 had an

increase of 15 years (or approximately that) in life expectancy. So that's obvious. It says that if people are really poor, they can't buy food, they can't buy health, they can't have a decent living environment, and they are going to die young. The other half of that curve is, What happens if people had vast amounts of money, 20,000 take-home dollars purchasing power a year in 1900? They still died on average 25 years earlier than people with \$4,000 income in 1990. What is it that with all the money in the world, you couldn't buy in 1900 but can buy in 1990? I would submit that a good part of that is knowledge--knowledge about health. A good part of that knowledge derives from science: antibiotics, drugs, public health, prevention of disease, ventilation, requirements for housing, occupational health. That is knowledge that you could not buy with money, and that's what science I believe has contributed to life expectancy in the modern era.

POLLACK: Barry, every one of those things you mentioned peaked before or around 1950. Name something from the second half of the 20th century which contributes to the same extent to an increase in life expectancy.

GRIFFIN: Early retirement.

BLOOM: The first real antibiotics were available in 1952. We have a lot more than penicillin now, and if you have a hospital infection in this modern world, with antibiotic resistance from many things, penicillin isn't going to get you through. We have a lot more vaccines; let me give you the numbers. Nine million kids that would have died in 1974 from vaccine-preventable diseases--when only 5 percent of the world's kids got the six vaccines--75 to 80 percent of those kids now get vaccinated, and 9 million don't die. That's knowledge.

POLLACK: You are making my argument. That is the expansion out of earlier ideas in basic science, and you're absolutely right: We should only have more of them. But I think the question we're being asked is, Will there be a qualitative new set of ideas from which applied biology and biotechnology can build, the way biotechnology is still building from the first half of the 20th century's notions of antibiotics, vaccines, public health, and clean water? Is there something out of DNA of equal power to a vaccine?

BLOOM: Sure. It's a fair question, and it's a common argument that all the ideas and fundamental advances were made in the past and now we're only cashing in on old investments in science, not the new science. Let's take the first exception. AIDS is a lethal disease; [AZT](#) came out of an ordinary drug screen, and it was pretty good, except that resistance developed quickly. We're going to have about 40 million people infected with AIDS by the end of this decade, and in the vast majority, 90 percent of whom live in developed countries, they are mostly going to die. What do we do for people here? Well, with [protease inhibitors](#) we saw the first example of rational drug design that I'm aware of: identifying a target for a drug, isolating the protein, making the crystal structure, modeling with the computer to get something that fits in the crystal structure. And then somebody--lots of somebodies--went out and made that. What's great is not that there was one drug, like penicillin, but there are eight or nine drugs, because they're all going to wear out sooner or later. That is the new paradigm. This didn't take 50 years from the idea to the product; it took



more like five.

BAZELL: And you're saying, to extrapolate this, that there's going to be lots of those in the next years.

BLOOM: There's going to be enough to make it wonderful, and an awful lot are never going to make it.

BAZELL: But the premise of this entire industry is exactly that: that all these targets can be so significant that they can be exploited.

GRIFFIN: I think there will be fragmentation. There's a vaccination policy to vaccinate the whole of the population, for example, against [poliomyelitis](#). I come from a period in the U.K. where I benefited directly from that, and I had relatives that did suffer from polio, and it was an awful disease. I don't think we're going to see anything as quite as dramatic or radical as that unless we get new diseases. I think there will be a fragmentation of the effort in biotechnology across a wide range of different issues, from environmental pollution through better veterinary care through treatment of very specific diseases. One of the problems that will have to be addressed is that if the market is fragmented into smaller sections, is there enough finance there available for companies to pursue relatively small markets? There are schemes by which, for example, drug companies or the first producers of products will get [Orphan Drug](#) status, and that benefits their position financially. In the Third World, perhaps it should be part of the aid programs to address issues which are relevant to people [there]. But the technology tends to be expensive, and we will have to find different ways of financing it with relatively small markets for each segment.

POLLACK: Since you talk about financing, and since I find Barry's answer compelling, I guess it makes me wonder whether we can, as a country, continue on what I see as two divergent paths. To the extent Barry is correct, and this technology throws off novel pharmaceutical interventions which could have not existed by a random walk but required a logical database of 3-dimensional crystalline structure of proteins--when that happens in a country where one person in seven has no medical insurance and no access to any medical diagnostic or treatment facilities, except in an emergency or in a prison--at what point does the corporate world that produces those compounds have some obligation to help move the politics of the country to a place where everyone has roughly equal access, depending on their need for these kinds of compounds?

Right now, in a sense, the greater the success, the more the class difference between those who can buy and those who cannot buy makes this country look quite irrational in its investment policy. What is the point of not at some point having medical care be in some way a right, as it is in the U.K. and in most of the industrialized world, so that the fruits of this product are seen as available by right--even if that were to perturb the market that right now drives the production of these compounds?

BAZELL: Isn't that just a socialistic argument, that everybody should be for free medical care, or even access to medical care? What's that got to do with biotechnology?

BLOOM: It's going to be a roundabout answer, but I will give it the following try. We are dealing with diagnostics and cures for diseases. That is why I went into biomedical

research: I cared about understanding diseases and finding interventions to treat them. I think we're in a new paradigm shift--prevention of disease; I hope biotechnology helps in that. I think we're going to come reasonably close in the next decade or two to how long people can live, functionally and usefully. And I gave you some figures on life expectancy; I would be able to give you some more on the equity question that Bob raised, if you wished. But I think that's not where we are going. I think we are going to a different world where life expectancy is not the measure, and I point out to you that in the health statistics in the United States, up until two years ago, the only index of health was how long you lived. Whether you were unable to function, in mortal pain, and destitute, was not part of those figures.

What one wants to do, and it seems to me the object of this paradigm shift basically is to prevent disease and disability to keep people alive, well, and functional to the day before they die. That is a paradigm shift, and when Bob talks about boutique medicine, I think that is correct; that is how we do it, and there will be an extent to which we'll have to do it. But there are also possibilities for prevention, and I'd to give you one, which again he alluded to. I think it's a profound change, and I confess the media has not missed it. It's a drug called [tamoxifen](#). We all know tamoxifen as an inhibitor of the estrogen receptor, which is a major treatment in breast cancer. But if you remember about two months ago in the newspapers there was a study indicating that people who had high risk but not breast cancer were treated with this drug, which was invented as a curative drug.

BAZELL: It was actually invented as a birth control pill by the company that is now [Zeneca](#), and this is an interesting saga. It was a lousy birth control pill; in fact, it caused multiple births, and it was put on the shelf. A guy named Arthur Walpole saw its potential, and he had a young graduate student at the University of Leeds named [Craig Jordan](#). He thought about the breast cancer problem and he said to Jordan, "Well, why don't you look at this as a potential for treating breast cancer?" and he used mammary cancer in rats as a model. So continue with your story.

BLOOM: In any case, what the article in the *Times* did was to show that this is now the first new cancer preventive that I'm aware of. If you talk to Harold Varmus, director at [NIH](#), he will tell you it's not a fluke. There are 70 trials now using anti-cancer drugs to prevent cancer at high risk. Then, how do you make new drugs, derivatives of drugs? I will tell you that combinatorial chemistry, which is related to biotechnology, is a way to make 50,000 compounds a week in a small one-floor biotech rented space in Cambridge or in Palo Alto--



Emerging technologies in history:
The Wright brothers

POLLACK: Or [Washington Heights](#).

BLOOM: Washington Heights, even. Whereas it would be five years before a major pharmaceutical company 10 years ago could make 50,000 derivatives of a lead-off compound that might work. I think that what we're seeing now is potentially a shift--one that could not be done by old-fashioned random screening--to create things that say, "We know what the tumor suppressor gene that's mutated in this kind of cancer; we can now make a crystal and design a drug." And not just give it to people with cancer and make a lot of money. If you had your genome analyzed to see that you had the wrong [p53](#) mutations, would you pay

to have a drug to prevent colon cancer, even though it won't work 100 percent of the time? And you might never get colon cancer? I sure as hell would.

BAZELL: Well, that wasn't missed. Eli Lilly then made a derivative drug, [raloxifene](#). These drugs are called selective estrogen receptor inhibitors; there are probably about 30 of them in the pipeline because of the tamoxifen success. What's interesting is that so far the market hasn't been there as a preventive. Tamoxifen has some side effects that causes some increases in uterine cancer and blood clots in the veins; raloxifene hasn't been tested long enough, and neither one is a treatment for osteoporosis. But that particular area, understanding the estrogen receptor in all its ways and turning out molecules, has been one of the most exciting areas of biotechnology, and we include in biotechnology big drug companies adopting the technology that we ascribe to small companies as well.

POLLACK: I think that's a comprehensive and good counter example. My contribution to this discussion, then, remains the wish to set a frame around such a positive answer, and that frame, I would argue, is political. It is a matter of equity. It's a matter of boundary conditions so that when we know from the data Barry speaks of that there is an interventional preventive way to keep tens of thousands of cancers from ever appearing, and the market does not see that as a thing to go for, nevertheless that's available. Now that is, you can say, socialism. Well, in this country, when you count federal, state, local employees, and the military, and veterans, half the people are on government medical insurance anyway. It's the other half that includes the one in seven that don't have anything. It's a crazy and irrational situation, and it prevents rational politics from accompanying rational drug design. A national DNA databank, to contain the kind of information you need to know whether you are eligible for such a drug, makes no sense when there's no national health service. So I would agree with you; I hope you're right. I hope to see how Varmus' combinometrics produced a thousand drugs. But we as a society are not prepared to distribute them equitably by biotechnology.

BAZELL: Isn't it in the interest of the sponsors of these drugs and the companies that are making them to do what Bob is talking about and make them available? We're seeing AIDS drugs that we were talking about only a few years ago as something nobody could afford. Now almost every person with AIDS in the United States is getting them, and we're starting to see them, amazingly, get into the Third World, despite what naysayers were saying. With the case of AZT for pregnant women, it's going to happen very soon, and it will probably happen with other drugs as well. And the reason it's going to happen, I would posit, is that people are going to make a profit. Isn't it in the interest of people who sell these things to make that happen?

The reasons for genetic information:
knowing, but not merely knowing



GRIFFIN: I'm not sure I wanted to be seen as a supporter of that sort of activity. That's certainly not my personal background. I think we've got a confusion here. If you want to introduce access to health care, access to employment, access to good education, these are all things which influence health. Again, I'm not quite sure why you should select a particular drug treatment as one that is going to distinguish between those people who can afford it and those who can't. Presumably, all those additional issues, good nutrition and education and so on, influence people's health. You mentioned socialism; there is more of it about in Europe than there is here, and I personally feel reassured by the fact that I have access to health care--not free access, but free at point of access. Irrespective



Emerging technologies in history:
Alan B. Shepard

of what I have inherited from my mother and father, genes which have predisposed me to illness or not, I have the same access as everybody else. I think that's a sensible part of national insurance. The idea that we're going to start distinguishing between people according to the genes that they inherit, I think, is a trend which should be resisted. I think each of us should be valued for what we are as an individual, not the genes that we carry.

BLOOM: I think there are really two issues, and I would like to ask the question and not answer it. To what extent does biotechnology have, in fact, an influence on the issue of equity? The numbers, I would hope, would outrage you. The country in the world with the longest life expectancy, just to take the simplest numbers, is Japan, with a life expectancy in 1990 of about 79 to 80 years. The country with the shortest is Sierra Leone, which has a life

expectancy of 35 years less. So if you are born in Japan, you're going to live 35 years on average more than if you happen to be born in Sierra Leone. So we sit back and say we could guess that. The exact numbers aren't important. And we say, "That's the Third World's problem. It's not our problem." Let me tell you: It is your problem.

There is a study released by CDC last week, the U.S. Burden of Disease and Injury study,² in which [Christopher Murray](#) at the Harvard School of Public Health has analyzed life expectancy, not in Sierra Leone, not in Mali, but in the United States of America by county. The bottom line is that if you are born in a rural county in Minnesota or Wisconsin or Colorado, your life expectancy will be 20 to 25 years more than if you're born in the county of Baltimore, or in the county of Washington, D.C., or in six counties in Mississippi, or a dozen counties in Alabama, or four counties in Idaho with the American Indians. That's a 20-year disparity in life expectancy in the richest country in the world. I think Bob Pollack's argument is right, and how do you get to be able to rectify that? First, you have to understand *why* there's a difference in life expectancy; we haven't a clue, because no one has done that kind of research, and my guess is the Indians in Idaho will be dying of things very differently than the people in Baltimore or in Washington.

I think the second question which I don't have the answer to is, Can you drive the equity when you have drugs that deal with all kinds of diseases, and in such numbers that everybody would profit if they were made available to the vast majority of people in the vast majority of counties?

That's what I see the biotechnology revolution--if greed doesn't overwhelm it--to be able to contribute. Because the imagination and the opportunities are there. How they will be used and made available around the world is our problem.



Emerging technologies in history:
Edwin "Buzz" Aldrin, Apollo 11

BAZELL: But isn't part of the problem that people are dying of gunshot wounds in some of those counties? People are dying of alcoholism in some of those counties, and it becomes fanciful to think that biotechnology has anything whatsoever to do with those deaths.

BLOOM: There's a great geneticist named [David Botstein](#), whom I think we all have known, a really marvelous geneticist, and once many years ago my school wanted to recruit him, because he was actually born in the Bronx. (We didn't have much luck; he's now head of genetics at Stanford and doing spectacularly well.) He came 15 years ago, when there was the excitement of finding out what genes caused Huntington's chorea and a whole slew of obscure neurologic and other diseases. I said: "That's not really very interesting. What do you really want to do with genetics?" And he said, "You know what I want to do? I want to do the genetics of the battered child syndrome." That is to say, Bob may resist it, but there is some genetic component to alcoholism, probably to violence, to illness and everything. Not that there is a gene for it; these are multiple traits; but we can gain some insight, and maybe some pills that would help control that for society, if we had more scientific knowledge.

POLLACK: Why would I want to resist that? What I would resist is the idea that such information be made available at a time when there is profit to be made by sorting out the risk if you are an insurance company. So long as you can use that information to set premiums, you can box out people and put them on a positive feedback loop, a downward spiral of absence of support. My argument is that any genetic information about our species has to be framed by reinforcement of the rights of a person, regardless of their



Emerging technologies in history:
Francis Crick and James D. Watson

secrets. Privacy and the meaning of the secrets to one's pursuit of happiness have to be protected explicitly, because they are implicitly not protected. So I think, terrific, if there's a genetic component to any aspect of human behavior, it can't be hidden. It will be known. The issue for technology, and the issue for any citizen of any civilized country, is to protect one's citizenship from bad consequences of knowledge of what one has been born with. This is not an argument for not knowing. It's an argument for not *merely* knowing.

BAZELL: But merely knowing is, as you said, where we are.

POLLACK: You called it pessimistic; I think we're in an early enough time for us to deflect this in a more positive way by acknowledging the problem. I'm not pessimistic; I'm concerned. It's an amber light I am trying to shed, not a red one.

BAZELL: Do you think that there's profit to be made, Harry, in complex trait analysis? You are trying to put proteins into mammary glands; you're not trying to find out why somebody becomes a compulsive gambler, with Dolly the sheep.

GRIFFIN: No, but part of our other work is to identify complex traits like growth or milk yield or behavioral traits in farm animals. And I think what's mildly amusing about some of the coverage in the press is the idea, for example, that people have found a gene that gives you perhaps two or three percentage points on the IQ test. I think most of you would think that in fact people have identified the gene from that sort of report. The reality is that the statistical methods used perhaps will indicate that there is a gene somewhere on chromosome number 27, perhaps towards this end rather than that end. There may be two or three hundred or perhaps a thousand genes in that region. And most of the traits that people are interested in, in this sort of context, are much more complex than is

commonly presented.

BAZELL: We have some brilliant students here. What is going to be different for them in terms of the practice of biology--if that's what they choose to do--from what has been in your career?

The next generation:
entering a field in mid-revolution



POLLACK: I'd like to answer that as a person who went to college, studied physics, got a Ph.D. in biology, worked as a professor in three medical schools, worked at [Cold Spring Harbor](#) with James Watson, came to Columbia, became a dean, and now writes books. I have had, you might say, an inability to hold a job for a very long time. And you will all have that obligation to not hold one job, I would say. The great success that you will have is in the flexibility of finding ways to use your intelligence and not be strapped to a technology of the past.

I decided a few years ago no longer to run my laboratory, because I saw the obligation of following the technology as occupying too much of my time. But I think the gift of youth is that the technology that to me is too much bother to learn is the first technology you'll learn. And you should not be tied to it. You should, I think, lead this revolution by putting the primacy of ideas in front of the attractions of any single technology. If you change your careers five times, as I did, I think that will be all to the good. If you don't, you'll be working for somebody else and doing what you're told.

GRIFFIN: One of the challenges in the future is to be able to combine disciplines. Biotechnology is one of those areas where you need a combination of skills--certainly, in our field, an ability as a molecular biologist to understand bioinformatics. Very different skills and expertise are something that we would treasure. Besides moving with the technologies as they develop, an ability to span from one technology to another is going to be a of great help for new scientists.



Emerging technologies in history:
Thomas A. Edison

BLOOM: I don't know why I'm into atom bomb metaphors today, but [Leo Szilard](#) has this wonderful line that says, "An optimist is someone who believes the future is uncertain." That's why you go into science: the curiosity about what you don't know. That is one of the great human gifts for people who have it, who just want to go and follow their nose and do experiments. If I were to give advice, it's very hard to go into work in a bank (I think; I've never worked in a bank) and get up in the morning and decide I'm going to do

something new and different every day. That's what I do. I've done that for 36 years. Every day is a new day, and I can't imagine any other way to make a living, or even not make a living. I can't imagine doing anything else.

Things are so fast, things are so automated--with pressures for profits and whatever--that you can lose the most important thing in science, and that is simply the wonder of this universe. If you keep that wonder, it's what keeps you going. The enthusiasm, the excitement, when 99 experiments fail and that one dinky experiment gets you to the next level: That's worth the whole year, and that's the wonder of science. I would urge people to sit down once in a while and say, "Do I really appreciate this universe?"

Related links...

- [Biotechnology Timeline](#), North Carolina Biotechnology Center
- [BioTech's Life Science Dictionary](#)
- [Council for Responsible Genetics](#)
- [Interview with Dr. Barry Bloom](#), excerpted from "Winding Your Way through DNA" symposium, UC San Francisco, 1992
- [Horace Judson, *Eighth Day of Creation*](#)
- [Eric Grace, *Biotechnology Unzipped: Promises and Realities*](#) (reviewed by Kemal Ahson in *Public Understanding of Science* 7.3, July 1998)
- [David Rotman, "The Next Biotech Harvest," *Technology Review* Sept.-Oct. 1998](#)
- [Steve Jones, "In the Genetic Toyshop"](#) (multiple book review), *New York Review of Books*, April 23, 1998
- [Shannon Brownlee, "Dollars for DNA"](#) (on profit potential of biotech), *U. S. News and World Report*, May 25, 1998
- [Students for Alternatives to Genetic Engineering](#)

1. World Bank: *World Development Report 1993: Investing in Health*. NY: Oxford University Press, 1993. Figure 1.9. Adapted from Preston SH, Keyfitz N, Schoen R: *Causes of Death: Life Tables for National Populations*. NY: Seminar Press, 1972.

2. Murray CJL, Michaud CM, McKenna MT, Marks JS. *U.S. Patterns of Mortality by County and Race: 1965-1994*. U.S. Burden of Disease and Injury Monograph Series. Cambridge and Atlanta: Harvard School of Public Health and Centers for Disease Control and Prevention, 1998.

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