

JAMES BONNER (1910-1996)

INTERVIEWED BY GRAHAM BERRY

March 13-14, 1980



Subject area

Biology

Abstract

Interview in 1980 with professor of biology James Bonner begins with his recollections of growing up in an academic family. In 1929, his father, a physical chemist at the University of Utah, was a visitor at Caltech, where Bonner enrolled as a junior. Recalls course work with X-ray crystallographer Roscoe G. Dickinson and activities of Division of Chemistry and Chemical Engineering under Arthur Amos Noyes; humanities courses with William B. Munro; physics with Earnest Watson, William V. Houston, and Carl Anderson; geology with John P. Buwalda; and biology with Thomas Hunt Morgan, Henry Borsook, and Theodosius Dobzhansky. Became Dobzhansky's summer researcher and editor; switched from chemistry to biology. Graduate work with Dobzhansky on *Drosophila* genetics and Kenneth Thimann on plant hormone auxin. Friendship with Noyes. NRC postdoctoral fellowship to Utrecht, Leiden, and ETH, 1934-35. Joined Caltech's Biology Division in 1936 as an instructor: recalls colleagues Frits Went, Arie J. Haagen-Smit, Johannes van Overbeek; plant labs at Caltech; coining of term *phytotron*. Recollections of Robert A. Millikan. War work for

U.S. Emergency Rubber Project on guayule and *Cryptostegia*. Work on cell biology with Sam Wildman; discovery of Fraction 1, central enzyme of photosynthesis. Founding of Caltech's Industrial Associates program in 1950. Recalls graduate student Paul Tso, discovery of plant actomycin, isolation of ribosomes. Work of Robert Holley on transfer RNAs. Consultant to Malaysian rubber industry. "Next 100 Years" project, with Harrison Brown. Studies RNA in 1960s with R. C. Huang and histone chemistry with Douglas Fambrough. Visitor at Oxford, 1963. Remarks on underdeveloped countries. Study of population growth with H. Brown. Comments on his recent work on cloning genes, and visits to Singapore and China. His hopes for genetic engineering. Stint as acting chairman of the Biology Division; comments on Robert L. Sinsheimer. [See also 1978 joint interview with Bonner, N. H. Horowitz, D. F. Poulson, and S. H. Emerson.]

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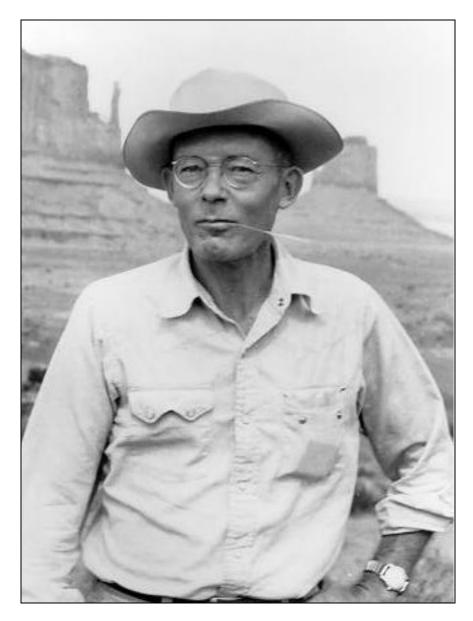
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James Bonner, 1950s

California Institute of Technology Oral History Project

Interview with James F. Bonner

by Graham Berry

Pasadena, California

Caltech Archives, 1982

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Errata

p. 4: "The book was *Chemical Principles*, by Arthur Amos Noyes (actually Noyes and Sherill)"—Noyes's coauthor is Miles S. Sherrill.

p. 10 ff.: "...which we now know as anxin"—Correct spelling here and throughout is auxin.

"...fellow students, like Don Poulsen"—Correct spelling here and throughout is Poulson.

- p. 23: "isoprine"-Correct spelling is isoprene.
- p. 24: "National Institute of Health"-Should be Institutes.

p. 39-40: "RNA polimerage"—Correct spelling is RNA polymerase.

p. 46-7: "Keiji Marushigi"—Correct spelling is Marushige.

p. 47: "octanemic"—Correct spelling is octameric.

p. 53-4: "afalatoxin"—Correct spelling is aflatoxin.

TABLE OF CONTENTS

Interview with James F. Bonner

Session 1

Childhood and early education: a family of chemists; Father's sabbatical at Caltech; James becomes Caltech undergraduate; Roscoe Dickinson and Linus Pauling; life in the chemistry department; William Bennett Munro; William Vermillion Houston; geology seems appealing; introduction to biology; Thomas Hunt Morgan and Theodosius Dobzhansky; memorable colleagues; decides on graduate work in biology; Drosophila genetics and plant hormones.

Physical and intellectual isolation of the biology department; biology faculty and fellow graduate students: E. G. Anderson, Sterling Emerson, George Wells Beadle; awarded National Council Research Fellowship to Utrecht: work in colloid chemistry; European visits; offered and accepts instructorship at Caltech: Biology 1; seeds of modern biochemical plant biology; early labs and naming of the phytotron; Dr. Millikan; Bonner Travel Endowment established. 19-29

Becomes full professor with tenure in 1946; Emergency Rubber Project and guayule research; more wartime rubber research; developing cell biology with Sam Wildman; discovery of Fraction 1 protein; learning from Paul Ang Pang Tso; protein research; messenger RNA; Bob Holly isolates transfer RNA; formation of the Industrial Associates Program. 29-36

Work with Malaysia Rubber Research and Development Board; industry - Caltech relations: Thomas Watson, Jr, and Sr., and the Caltech Computing Center; "The Next Hundred Years" seminar; predictions: hit and miss; developing vs. developed countries; Commonwealth Agricultural Conference (Australia, 1949).

Session 2

37-54

Skiing styles; joining the ski patrol; 1960 work on how RNA is made: histone chemistry and the First World Conference on Histone Biology and Chemistry; histone sequencing; trip to Nepal and the story of the yak's tail; twice around the world, or pairing the spin; Eastman Visiting Professor at Oxford; 1967: "The Next Ninety Years;" 1968: continues research into gene expression; trip to South America and Africa; interest in study of population growth and developing countries. 54-69

American Universities Field Service; Singapore; recombinant gene technology; trip to northwest China in 1979; genetic lottery; Robert Sinsheimer; ongoing projects.

1-10

CALIFORNIA INSTITUTE OF TECHNOLOGY

ORAL HISTORY PROJECT

Interview with James F. Bonner Pasadena, California by Graham Berry

 Session 1
 March 13, 1980

 Session 2
 March 14, 1980

Session 1 Begin Tape 1, Side 1

Bonner: I came from a family of seven children. I was the oldest child. My father was a physical chemist and got his Ph.D. at the University of Toronto in Canada. And his father in turn had been a Scots Presbyterian minister who had emigrated to the United States and found out he couldn't make a living as a minister, and so he started farming in Nebraska. He got his 140 acres and made, I guess, a fairly miserable living; he ministered on Sunday and the rest of the time he farmed. I remember my father telling me about how terrible those early years were and how he hated oxen, because he had to hitch up the oxen and drive in to town on Saturday and take in whatever they'd raised and sell it. And in his oldest years, when he was beginning to lose his memory, he would say to me, "Son, let's hitch up the oxen and go to the laboratory."

Anyway, my mother and father both grew up on farms in Nebraska. And they both ran away from home and went to Nebraska Wesleyan University, where a young man named Frederick Alway, who had recently gotten his Ph.D. in Germany--which was the haven for all chemists then--had come to teach. And he taught a vast number of people at Nebraska Wesleyan University in Lincoln, Nebraska, to become chemists. My father had gone first to Princeton, where he thought he wanted to be an organic chemist; and then when he wanted to be a physical chemist, he went to Toronto. He then got a job at Queen's University in Kingston, Ontario. And that's where I spent the first five years of my life. I was born in Ansley, Nebraska, on a vacation trip; that was my mother's home town. When I was six weeks old I went back to Kingston. My next brother, Lyman, and my sister, Priscilla, were both born in Kingston. It was in Kingston that I first remember thinking that everybody in the world was a chemist because that's all my parents talked about. We didn't go to church, of course, because my father hated his father so much that he decided to be an atheist, and he decided that religion was too dangerous for children to be exposed to it. We were not only forbidden to go to church or Sunday school, we didn't even discuss religious matters. And my father wouldn't discuss them until we reached the age of reason, which he defined as sixteen years old. By that time, we were committed to not going to church, of course. So I didn't have to learn anything about church matters.

I went to grade school, and I didn't do particularly well because my mother thought she knew more about teaching than any other ordinary teacher. She taught me at home until I was eight years old and then inserted me into the fourth grade, which I was too young for. I had a terrible time; that's why I never learned to write properly. And I remember being totally mystified, seeing children sing music, looking at strange scribblings, which we now call music notes, in a book, and I couldn't figure that out, and never did.

Then I went to junior high school, and during junior high school my father took a sabbatical leave from the University of Utah, to which he had moved when I was five years old, where he became chairman of the chemistry department. His sabbatical leave was at the University of California at Berkeley. And there, all of a sudden, I learned a great deal about mathematics very rapidly. I must have been just old enough to learn about mathematics. I remember I was at Helen Wills Junior High School, and Helen Wills, who was a tennis great of the olden days, had gone to that junior high school. And my brother Lyman and I took bicycle trips to the Muir Woods--you could still do that from Berkeley in those days. It was still safe to ride bicycles on highways. And we would take our bicycles and go down and cross the bay on ferry boats innumerable times. It was really fun. My father met a young graduate at Berkeley--this was in 1922, '23--and this undergraduate was Don Yost. My father was very impressed with Don, who was a chemistry undergraduate, and later on persuaded Don to come to the University of Utah to be a graduate student, where he got his

master's degree in chemistry, which was as high a degree as was offered at the University of Utah at that time. Parenthetically, my father had started the graduate school at the University of Utah. Finally, right after the end of the Second World War, they got around to creating a Ph.D. granting program at the university, and the first graduate student to get his Ph.D. was of course a chemist who had done his graduate work with my father.

Well, my mother didn't stay so implacably enmeshed in education for all her other children. Lyman, who is two years younger than I am, went to school. He started in the second grade, and then from there on, everybody started in either the first grade or kindergarten, like ordinary people. Anyway, as a result of my head start in school, and as a result of Lyman's head start in school, we both finished college at a rather early age and finished graduate school at a rather early age, as I will come to in a minute. Somehow, subtly, all seven of us children were turned into chemists. I think it just never occurred to us that there was anything else that one could be. Even after I'd learned that there are people whose parents were lawyers and such like things, my parents made it clear that they were a lower order of humanity than us chemists. And the only thing that bore any dignity other than being a chemist was to be a mathematician; and that didn't seem like so much fun. I'd already started learning how to wash test tubes and make up solutions when I was six. My father took me to the laboratory and taught me how to do such things. And I started learning glass blowing and all that; and mathematicians can't do that. It just automatically turned out that all seven of my parents' children, my six siblings and myself, got their bachelors' degrees in chemistry. I got my bachelor's degree in chemistry with a minor in mathematics, and I still like mathematics very much.

In the meantime, another event of great importance had happened. Don Yost had gotten his master's degree at the University of Utah, and my father recommended that he go to the new Caltech in Pasadena for graduate study. My father recommended this because he was a physical chemist, and Don wanted to be a physical chemist. My father knew Arthur Amos Noyes, who was chairman of the chemistry division and one of the cofounders of Caltech, and admired him very much as a father of modern physical chemistry in the U.S., which he was. So he sent Don Yost there. And Don Yost had not only gotten his Ph.D. at Caltech, he'd gotten a postdoctoral fellowship to go to Sweden and come back and become a faculty member at Caltech--he was an outstanding experimentalist. So my father took his next sabbatical leave at Caltech. His entire family came to Pasadena in 1929. This was the year that I should have been a junior in college, but I decided to take the challenge and come to Caltech also. And Dr. Noyes arranged for Lyman and myself to have fellowships to be undergraduates at Caltech, provided that we took the entrance exams and passed them with high enough scores, which we did, of course.

So we became Caltech undergraduates. This was the beginning of a whole new insight into life. My advisor, interestingly enough--all Caltech undergraduates have advisors--my advisor was Linus Pauling, who had just returned from a postdoctoral fellowship overseas, and who had started to work on crystallography, which he had learned in turn from Roscoe Dickinson, who was a professor of chemistry, and who was the first Ph.D. from Caltech. Roscoe was a real, honest-to-God, good, X-ray crystallographer, and he's the man who taught Linus Pauling X-ray crystallography. Linus still celebrates him, and in his history of chemistry in the U.S., he gives great credit to Roscoe Dickinson as being the first person in the United States to establish the crystal structure of a substance by X-ray crystallography.

Now, as a junior at Caltech, I had to take some courses, like Chemistry 21, Physical Chemistry--the dreaded nemesis of all upperclassmen. But Chemistry 21 was taught by Roscoe Dickinson, and it was really a breeze. I and another fellow in the class, who didn't amount to anything subsequently, vied with one another to get the one "A" that Roscoe was going to give in the course; I beat my competitor out, and I got the "A" each term for three terms. That was an interesting course because it was the first one I'd had where you couldn't learn anything by rote. The book was <u>Chemical Principles</u> by Arthur Amos Noyes (actually Noyes and Sherill). It consisted of problems, and you couldn't work the next problem until you'd totally really understood the first problem; you couldn't fool yourself. This was a new way of thinking. It really appealed to me and made me really want to be a physical chemist and understand things right. A second aspect of life in the chemistry division was that Dr. Noyes had an unbreakable tradition that Tuesday and Thursday at 10:00 a.m., all chemists had to get together and they had a class. The class was taught by the professors, and they'd take a subject like thermodynamics or infrared spectroscopy or quantum mechanics and just absolutely beat it to death, very, very thoroughly. It had to be attended by all the faculty, all the postdoctoral fellows, all the graduate students and all the upper-level undergraduates. Т went to that class during the time that I was an undergraduate; and I went to it all the time that I was a graduate student and for several years after I became a faculty member at Caltech. It was an excellent class. And parenthetically, it was this class that taught Howard Lucas-an organic chemist who didn't know beans about electrons or what a covalent bond was--taught him about both of those things. And Howard Lucas transformed organic chemistry from a cookbook science to a modern science with predictive value. And he wrote a classical, what we would call physical/organic chemistry textbook, which became a standard text for teaching organic chemistry. And he taught outstanding graduate students in organic chemistry, the best one of whom went to UCLA and had a graduate student named Jack Roberts, who subsequently came back to Caltech and continued the great tradition of eminence of Caltech in organic chemistry. This was interesting because Dr. Noyes looked down his nose at organic chemistry and thought there was nothing more despicable than to be an organic chemist, if you were going to be a chemist at all.

So that's one thing I learned, that physical chemistry is great stuff. I also had to take some humanity courses because at Caltech, they're big on having humanities. And at the University of Utah, I didn't have to take very much. So I had European history from William Bennett Munro, chairman of the humanities division for years and years. He'd come from Harvard; we called him "three-button Benny," a real stuffed shirt. But he was an excellent teacher, and I will always remember his describing communism and explaining theories of Marxist dogma. He would put his hands in his vest pocket and rock back and forth on his heels and toes, mimicking Dr. [Robert] Millikan and saying, "If I were a Marxist, this is what I would say," and trying his best to behave like a Marxist, which was very difficult for him.

I also had to take freshman physics, because I hadn't had any physics.

We had an honor section in those days, and I was in an honor section. This was a very, very good class. It had William Vermillion Houston, professor of physics, as the TA who taught the problems section. We had lectures once a week by Professor Watson, who incidentally, I had seen while I was in high school. He went around the country giving a demonstration of liquid air, in which he would freeze a goldfish and either shatter one of them or put the other one in water and pretty soon it would thaw out and swim away. He made a great impression on me. He gave the lectures, and William Vermillion Houston taught us how to solve physics problems. Students hated him so much that they petitioned the administration to get rid of him. So he was succeeded by Carl Anderson. And Carl Anderson was, I guess, an instructor at the time; he'd just gotten his degree. Anyway, during the course of Physics 1, he got awarded the Nobel Prize for his discovery of the positron; and after a suitably decorous length of time--I would think it was about three or four or five months--he was promoted to being an assistant professor on account of this. Really got a great reward. Dr. Millikan already had his Nobel Prize, and there were lots more to come.

Another thing I had to take because it was required at Caltech-everything at Caltech in those good old days was required; you didn't have any options at all--I had to take geology. Lectures were given by John Peter Buwalda, who was another big stuffed shirt. But as it turned out, it was an extremely interesting course, and I really loved it. It made me think that I wanted to be a geologist. So I worked for one summer for a geologist; and I learned that being a geologist entails just walking up and down mountains, putting rocks in your pocket. It was extremely dull, and so I decided not to be a geologist.

Another course I had to take as an undergraduate was the required course in beginning biology. This was taught by Thomas Hunt Morgan, who gave half of the course and told us about genetics, and by Henry Borsook, who was an assistant professor of biochemistry, who told us about enzymes and interesting chemical aspects of biology. It was a really good course. It opened my eyes to the fact that there is such a subject as biology, which at the University of Utah was nothing. The most stressed field at Utah was spider taxonomy. My father had always told me, and I believed him implicitly, that the only thing that's more despicable than biology

is education. And he just hated the school of education. I never had anything to do with biology and never took any biology course at the University of Utah. This course showed me that genetics is fascinating, and that enzymology is not so bad either. The man in charge of the laboratory of Biology 1 was Theodosius Dobzhansky, who was a Russian who'd received his Ph.D. in genetics at the University of Kiev and had come to Columbia to be a postdoctoral fellow with Morgan, but just a few months before Morgan moved to Caltech. So Morgan said, "Come along, and you can come to Caltech; and after you finish your fellowship, I'll make you an assistant professor"--that's the way things happened in those days, very informal, nothing on paper. So Dobzhansky came along in 1928, and he was put in charge of the laboratory for this course, which I took in the winter term of 1929. It was excellent, and Dobzhansky was a really exciting guy, an excellent teacher, and a great turner-on of people. So when a second biology course was offered for the next term, the spring term, I took that, too, and I learned a lot about cytology--that is, looking at chromosomes in a microscope--and I learned some things I didn't want to know about, like how to dissect frogs and so forth.

Dobzhansky made me the proposition that I should stay in the summer and be a summer undergraduate research assistant for him. I did this, and the work went somewhat as follows: my principal duty was to take Dobzhansky's manuscripts--he believed that if he didn't write one paper a month he was wasting his time, so he always had lots of manuscripts-and I would take the manuscripts and translate his Russianized English into real English. And the rest of the time I learned classical genetics, how to locate the breakage points of translocations, and the breakage points of inversions, and how to look for new mutations, and how to collect virgin Drosophila -- no easy trick, collecting virgins. And then we would work for three or four days, and Dobzhansky would say, "Now we've worked very hard. I think it's time that we take a day off and go to the beach." So we'd go to the beach and swim and have fun. And after we'd done a couple of weeks of such hard work like that, with only going to the beach once or twice, he would say, "I think we've worked hard enough, now it's time to go to the mountains for a camping trip," and so we'd go to the mountains for a camping trip. And I thought the life of a biologist is really nice, because this never happened to me while I was being a chemist. I really got to think seriously about biology. That was a really important influence in my life, because if it hadn't been for coming to Caltech and being exposed to Morgan and Dobzhansky, I never would have made the switch. Anyway, the Depression started, and Caltech became very hard-up for money, and Dr. Noyes couldn't offer me a fellowship for a second year. So at the end of September 1930 I went back to the University of Utah and got my bachelor's degree as quickly as I could, and immediately came back to Caltech and started working for Dobzhansky again.

Berry: Do you have any recollections about your fellow students that you want to mention? You worked very hard while you were there.

Bonner: Sure, but I do remember some of my fellow students. One of them was my brother Lyman. Lyman got into a bad set of colleagues who played all the time and drove their cars fast; and he flunked out of Caltech and was told to go away and never show his face again. So this challenge caused him to study very hard for two years at the University of Utah so that he could get admitted to Caltech as a graduate student, which he was. And he did get his degree also from Caltech, a degree in physical chemistry (his advisor was Professor Badger). So he was one. Another important student in my Physics 1 class was the person who subsequently became the director of JPL (Jet Propulsion Laboratory)--William Pickering. He took Physics 1 just like any ordinary mortal. I was impressed by him because he had a New Zealand accent, and I had never heard one before. Little boys from Utah don't hear New Zealand accents all that frequently. There probably are some other undergraduates that I remember, but I'll talk more about the graduate students I met in a moment. One person with whom I became very friendly as an undergraduate was Dr. Tolman, Richard Chace Tolman, who was professor of chemistry and theoretical physics and cosmology. I had a little space to study in a corner of Don Yost's laboratory. Dr. Tolman had his office right around the corner, and he was always writing a book on cosmology at night. As we know, writing is very hard work, and he would always be leaving his writing to go to the nearest men's room and pee. I met him in there one time, and he told me wisely that it takes an awful lot of peeing to write

a book. Then both I and my father became very well acquainted and very friendly with Arnold Beckman, who also had his lab in his office. close to Don Yost's. I became even more acquainted with Arnold Beckman when I was a graduate student. We used to go out to him to get glass electrodes because he was working on how to make better glass so it would make better glass electrodes for better pH measurements. He found a good glass for making better pH measurements sometime in the early 1930s. We always measured the potential across a glass membrane, which had a standard concentration of HCl on the inside, and an unknown concentration of hydrogen ions on the outside -- so we measured that the junction potential with a wheat-stone bridge and a very sensitive galvanometer mounted on a concrete pillar so it wouldn't shake. Arnold Beckman had the idea of building a small amplifier so that you didn't have to have all this complicated equipment, but could determine what resistance you had to use to have the resistance in the amplifier equal the resistance of the glass electrode. I should put it another way: to have the EMF in the amplifier equal and be opposite to the EMF across the membrane caused by the two concentrations of hydrogen ions. This amplifier, together with the associate glass electrode, he called a pH-meter. Everybody in Caltech wanted one. He started making them in his garage, and pretty soon the demand became so great that he started building them in a building that he rented on Mission Street in South Pasadena; and pretty soon he resigned from Caltech; and pretty soon he became the two-hundredth largest corporation in America, which I guess he still is. We've stayed friends all these years.

So in the summer of 1931 I came back to Caltech. I'd applied for admission to the chemistry division and also applied for admission to the biology division. I guess I applied to the chemistry division because my father was so disgusted that I should consider going into biology. But I accepted admission into the biology department, and my father thought that I'd gone crazy. Of course, his opinion was shared by many people on the Caltech campus. Caltech had started in 1920, and this was already 1931; biology at Caltech was less than three years old. The general opinion is evidenced by a remark that I like to quote, made to me by a graduate student in physics (Willie Fowler, who will of course deny this), who said, "Biology? How are you ever going to make a science out of that?" And that's the way most people felt: that biology was just a bunch of facts and no science, nothing rigorous about it.

Anyway, I came and started to work with Dobzhansky on Drosophila genetics. I worked for about six months with Dobzhansky, and then I decided that there was some very interesting work going on, on trying to isolate a plant hormone. The first plant hormone that had ever been discovered had been discovered by F. W. Went, and it was being worked on at Caltech by Herman Dolk and by Kenneth V. Thimann, who subsequently left Caltech to become a professor at Harvard. I worked with Thimann on trying to isolate this hormone, which ultimately was isolated. I split off from this problem to take on my own independent problems on finding out how the plant hormone, which we now know as anxin, does its work. I worked part time in genetics and part time on plant hormones, and went on Tuesday and Thursday at 10:00 to the chemistry class to learn more about chemistry. I had a busy time.

In the genetics laboratory, [A. H.] Sturtevant and Dobzhansky had tried to recreate the famous fly room of Columbia. They sat at the two ends of the long table and looked at their flies. The students sat in between and listened to the wise conversation and contributed to it when they could. So I sat at this bench with my fellow students, like Don Poulsen, who is now a professor at Yale, a Drosophila geneticist. We were given a list of things to read. Dr. Morgan was firmly against any graduate classes, and we didn't have any; we had, however, reading lists of things we had to read. And then we had seminars. There was a general biology seminar each Tuesday night, and Dr. Morgan would come and go to sleep during the seminar, and at the very end he would wake up and ask a sensible question because he'd really not been asleep all the time; he'd just had his eyes shut.

Begin Tape 1, Side 2

Bonner: I should mention another aspect of biological life at Caltech. The biology building--which was the first unit of Kerckhoff Laboratories-was built on the extreme northwest corner of the twenty-acre original Caltech campus, and was isolated, completely isolated, from all of the other buildings--from the administration building, Throop Hall and from the chemistry building, Gates Laboratory, and from the physics buildings across the quadrangle. It was all by itself. It was connected by a boardwalk to the rest of the campus. In the winter, the territory between Gates and Kerckhoff became a sea of mud, known generally on the campus as Lake Kerckhoff. So we were not only intellectually isolated from the rest of the campus pretty well, but also physically isolated. This didn't change until 1938, with the great building spree of 1938, which I'll come to in a little while.

I should mention also that Dr. Noyes continued to be a friend and discuss things with me intermittently. He told me many times about why he left MIT, of which he had been president when he came to Caltech. He said, "The trouble with MIT is that it's too large, and we must not let Caltech get to be too large. It should be just the size it is--200 new undergraduate students a year is enough." In addition to Dr. Sturtevant and Dr. Dobzhansky--Sturtevant, by the way, was the only full professor on the biology faculty, besides Dr. Morgan--in addition, there was a group of younger people, starting with E. G. Anderson, who was a corn geneticist. Corn had the best understood genetics of any creature except Drosophila by the end of the 1920s and 1930s. We had a farm, a ten-acre farm, in Temple City, and E. G. Anderson ran a gigantic corn genetics program. He gave a seminar for graduate students on In genetics, and we used to bicycle out there and go to the seminar. addition, Sterling Emerson, who is the son of the Emerson who had been a founder of corn genetics at Cornell University, was assistant professor. He worked on Drosophila genetics, and he also worked on the genetics of an obscure Oenothera organensis, which lives in the Organ Mountains in New Mexico and has interesting problems of self sterility. The first day that I returned from the University of Utah to become a graduate student, I bicycled out to the farm to see E. G. Anderson, and there I met a young man who was busily hoeing the weeds out of his corn patch. This turned out to be George Wells Beadle, whom I've known from that day in 1931 to this, and who ultimately became the chairman of the biology division, and who ultimately became the founder of biochemical genetics. Also, of course, there was K. [Kenneth] V. Thimann and Henry Borsook, whom I have mentioned, and Herman Dolk, assistant professor of plant physiology, who worked on plant hormones, and who got accidentally killed in an automobile

accident in 1932 and was replaced by Frits Went. Also a cytologist, whose name I've forgotten but I'll look up, a very famous cytologist who was also killed in an automobile accident when his Ford roadster flipped over when he was coming back from Monument Valley to Pasadena. We had a lot of automobile accidents in those bad old days. So amongst my colleagues as graduate students in biology was the aforementioned Don Poulsen, who was a Caltech undergraduate and then a graduate student who got his degree after me. And Emory Ellis who got his degree in biochemistry and who ultimately started working on bacteriophage and introduced Max Delbrück to working with bacteriophage--taught him the methodology. And Marston Sargent, who worked with another faculty member I haven't mentioned, Robert Emerson, who works on photosynthesis and who is one of the all-time great innovators in photosynthesis. He invented the photosynthetic unit, he redetermined the photosynthetic efficiency, the quantum efficiency of photosynthesis and got it right instead of wrong like Otto Warburg had. And that's interesting because Robert Emerson had done his graduate work with Otto Warburg in Berlin. But even so, he checked up on Otto's work and found it was wrong.

There just weren't very many graduate students. Some of us had the good fortune to be supported. I was a teaching fellow, and for the \$750 a year which I got as a teaching assistant, I had to give laboratory classes. I taught laboratory for microbiology, laboratory for an introductory Biology 1 course--all kinds of laboratory classes. I calculate that over the years, I've taught every class that's given in the division of biology or ever has been given, except neurophysiology. We used to teach cat anatomy; I never taught that either. One has a great opportunity to teach different things at Caltech.

In the winter of 1933-'34, Dr. Morgan mentioned to me informally, he said, "I think that next year you should go to Europe." Of course, it was still believed, in those far-off times, that you had to go to Europe as a postdoctoral fellow as a sort of finishing school, where you could learn what people in the great long-established schools knew and that Caltech was such a new place, it was good for us to go abroad; and almost all Caltech graduates that were expected to amount to anything did so. So anyway, Dr. Morgan mentioned this. And to my amazement, in April 193⁴, I got a letter from Professor William J. Robbins, chairman of the National Research Council Committee on Fellowships in Biology, announcing that I had been awarded a National Council Research Fellowship to work for one year in Europe--the exact subject of my investigations to be determined by consultations with Professor [Max W.] Gardner at the University of California. And my stipend would be the magnificent sum of \$1625 a year, plus traveling expenses. How marvelous!

I finished up my thesis, which of course is on file with all the other theses from Caltech, and after graduation, which I actually attended -- most people don't do it anymore, but I attended and got the hood hung on me--I took off in my Chevrolet roadster, a very worn out one, and went to Salt Lake City and took a short vacation visit with my family. And then I got on a Greyhound bus and went to New York, and then got on the Redstar Line Steamer, Penland, which was sunk during the Second World War, and went to Antwerp. From there I went by train to Utrecht, where I was to start work. In the meantime, I had discovered that one can't work in the summer in Europe because in Europe all the people take off during the summer and take summer vacations. So I had arranged to go early, arriving in early July. Since things wouldn't start up until September, I took a two-and-a-half month bicycle trip through Europe, just like people used to be supposed to do in the olden days: I bought a bicycle and saddle bags and traveled through Germany, Czechoslovakia, Austria, and Switzerland, and back through Germany and Belgium and Holland, with my bicycle. It was really great. I stayed in the student hostels. I got to listen to Hitler giving speeches, and I saw him give one in Munich (München), listen to his raving and ranting--very interesting.

This year in Europe was extremely productive. I worked for several months in the laboratory of colloid chemistry in the chemistry department of the University of Utrecht (Professor Kruyt). Colloid chemistry was a very respected part of chemistry at that time--it no longer is. So I decided to learn colloid chemistry because this looked like the route into understanding something about the nature of protoplasm. I learned a lot of good methodology, but I didn't really learn anything. I learned to speak Dutch very well, and I learned to write Dutch very well, and I published several papers in Dutch on subjects related to colloid chemistry. I forgot to say that I'd studied German as an undergraduate; and I was so impressed, when I got off the train in Berlin and started talking to people, that they could understand me and I could understand them. It turns out that learning a language isn't all bad; and learning German was one of the better things that I did as an undergraduate. It's been very useful ever since. Anyway, in Holland, I even kept my notebooks in Dutch. I really tried to get integrated. I got good enough so that the ticket seller in the Utrecht railway station, when I asked for a ticket to go someplace, would answer me in German--at least not in English. She never got around to answering me in Dutch.

Then I went to the department of biochemistry at the medical school in Leiden, because in Leiden there was a man named Bungenberg-Dejong, who was a sort of colloid chemist and who was the master of coacervates. Coacervates are things which happen when you mix two colloids in aqueous solution. They make a complex, which separates out as a separate phase from the water. This, he imagined, was a model of how protoplasm is made-but he was probably wrong. What I did there that was extremely interesting. A second problem which was suggested by Professor Bungenberg-Dejong was to try to make lipid bilayers. And I actually made lipid bilayers that made stable vesicles. And the paper, which I wrote together with him in 1934, is still cited as the first example of people making a lipid bilayer. This simulated both the structure and the properties of cell membranes. Great stuff!

I then had permission from the National Research Council to go in early spring to the Swiss Federal Institute of Technology--the ETH--where I wanted to learn more about how to be a biophysicist. The work in Zürich under the direction of A. Frey Wyssling concerned how to use a polarizing microscope to study the arrangement of macromolecules in biological structures. I learned a great deal about that; and I made some really relevant contributions to the study of plant cell walls, which are still quoted. I learned to be a pretty good biophysicist from the standpoint of the 1930s. Also, I got to practice my German a lot, because Zürich is in the German-speaking part of Switzerland; and although everybody speaks their own cantonal dialect, in the university we spoke High German; understandable standard German; understandable to everybody. There I wrote several papers in German. The net result of this year was I wrote something like twelve papers, just like Dobzhansky would have expected of me.

Bonner-15

Towards the end of the year, I made a whole lot of visits. I visited Italy extensively; I traveled to Germany several times to see Laibach in Köln (Cologne), who was an expert in the plant hormone field. In fact, I was in Germany on the day that Hitler marched into the Ruhr district, which had been demilitarized. He marched into the Ruhr, which he wasn't supposed to do, and nobody stopped him, and this encouraged him to go on to make the further steps, which ended up in the Second World War.

I went to a botanical congress which was held in Amsterdam at the end of 1935, where I made several lasting friends, particularly Professor Hiroshi Tamiya, professor of botany at Tokyo University, and one of the world's authorities on photosynthesis, with whom I have had a lasting friendship over all these years and continuing through the Second World War. I also took a flying visit to London, visiting the famous human physiology laboratories in London.

I got also a letter, offering me a job--only one letter, only one job. This was a letter from Professor Morgan, suggesting that I come back to Caltech and that I take up sort of an auxiliary instructorship. The salary would be \$1500 per year. I wanted to come back to Caltech, of course--there's no other place like it, as I knew then and I found out even more about this being true since--so I came back. I take pride in the fact that my salary never sank below \$1500 per year, which is better than Beadle did; his sank to \$1200 per year the next year. He was still there when I got back, although he left shortly after to go to Paris to work with Boris Ephrussi. Boris Ephrussi was a refugee from Russia, who'd gone to Paris and learned to be a tissue culturalist and had been sent by the Rockefeller Foundation to Caltech while I was a graduate student to learn to be a geneticist and had become France's outstanding geneticist. He then came back again, after my return from Europe, bringing a graduate student with him. This graduate student was Jacques Monod, of subsequent very great fame, who was then a graduate student at Caltech for about a year and a half before he returned to France and started the revolutionary discoveries on the regulation of gene expression in bacteria, which ended up in his getting a Nobel prize. Anyway, Beadle left Caltech with a fellowship, apparently supplied personally by Morgan, to go to work with Ephrussi to see if he could transplant tissue of one genetic constitution into Drosophila of a different genetic constitution,

and find substances that would travel from tissue to tissue and affect gene expression. And he in fact found them. This started him on the road to inventing biochemical genetics, of which more later.

Anyway, I came back and I found out that my chief duty, besides doing research, was to be in charge of the laboratory for Biology 1. I was in charge of the laboratory for Biology 1 for twelve successive years, after which I was in charge of teaching Biology 1 as well as being in charge of the laboratory; and I spent something like twenty years on this Biology 1 task. The only way that I finally got out of it was when I accepted an invitation to be the Eastman Visiting Professor at Oxford in 1963-1964, and the division had to find somebody else to teach Biology 1. So I got out of it. When I came back from the 1963-1964 expedition, I was given the task of teaching cell biology (Biology 9) which is the second course. And it ended up that the Biology 1 teacher didn't get tenure, left Caltech, and my course, Biology 9, was changed into Biology 1. And so here I am, in 1980, teaching Biology 1 again, right where I started in 1936.

Berry: I guess there's a lot of change in Biology 1.

Bonner: Oh, sure. It changed year by year. I made it a survey of what is interesting in biology. I did a lot of teaching during that time. I taught biochemistry part of the time for Borsook. And I taught advanced biochemistry, which was a very interesting course which lots of people took. I also--but Dr. Went deserves credit for this. Dr. Went invented, based on the Noyes principle, a Tuesday-and-Thursday-at-10:00 course for plant biologists. There was a great concentration of plant biologists at Caltech. The Caltech work on plant hormones had made a very great impression on the world. It was the first sort of biochemically inclined plant biology that had been done anywhere in the world that ever amounted to anything. And so we were inundated with visiting professors coming to get to learn about the great new science; we had lots of graduate students and lots of chemists as graduate students who wanted to take a minor in plant biology. It was really the home of modern biochemical plant biology.

It was also the home of something else. A. J. Haagen-Smit had joined the division of biology in 1936. He was the man that had discovered the chemical nature of the hormone anxin, and showed that it is indole-3-acetic acid. He showed this in Utrecht. He was then asked to come to Caltech and came, and was one of my closest colleagues for all these years. I first met him in Holland in 1934. I knew him continuously right up to his death a year or two ago. He switched from plant hormones to work on the chemical nature of smog, and is the greatest single contributor to the understanding of smog and to its amelioration. A great and modest man.

We had Johannes Van Overbeek, who also came from Utrecht and is one of the fathers of understanding of geotropism. He was an assistant professor of plant biology and a member of the plant group. So we had quite a big thing going, and, as I said, Caltech was really a world center of work in plant biology.

We did have unique facilities. We had, in the first place, the Dolk Laboratory, named in honor of Herman Dolk, which was without any gas supply, because in the olden days, gas, which was coal produced gas, contained ethylene, and plants can't stand ethylene; it causes odd responses. So we needed plants that didn't have any ethylene responses and a separate building without any gas was built for the purpose of plant hormone work. Subsequently, Southern California turned over to natural gas, which doesn't contain ethylene. So that laboratory, although it continued to exist, was not really needed so badly. Also, and this is a digression, beginning in 1936 Dr. Went became very interested in environmentally controlled greenhouses. He built and opened in 1938 two units, two greenhouses, side by side, which could be run at different temperatures, where he could begin to find out what are the aspects of climate which plants care about--like, is it the day temperature or the night temperature? One could shift plants between the two greenhouses and find out. This was followed subsequently by building the Earhart Plant Research Laboratory, which opened in 1949, which contained four more greenhouses, so that we had a total of six that could be run at six different temperature regimes, plus a total of almost twenty artificially lighted rooms that could be run under a wide variety of conditions. This was called an environmentally controlled greenhouse. But my first postdoctoral fellow [Sam Wildman] and I, sitting around about 1950, having coffee, decided it deserved a better or more euphonious name than environmentally controlled greenhouse; and we decided to call it a phytotron--phytos from the Greek word for plant, and tron as in cyclotron,

a big complicated machine. Went was originally enormously annoyed by this word. But Dr. Millikan took it right up, saying "This edifice financed by Mr. Earhart, is going to do for plant biology what the cyclotron has done for physics," and he christened it a phytotron. This word has now become international: it's even a phytotron in French; it's a phytotron in Russian; it's a phytotron in Japanese; in Chinese it's a phytotron, too. In every language in the world, a phytotron is a phytotron.

So I continued to work on plant hormones and finding new plant hormones. And I found out quite a number. I got promoted to be an assistant professor. It's interesting the way you got promoted. Dr. Millikan would call me up and say, "Come over and see me." And I would go over and see him, and he'd say, "Well, you're now an assistant professor." And this was never written down anywhere: I never had any contract with Caltech, nothing written on paper, I never had any salary arrangements. That was all between me and Dr. Millikan. And from time to time he would call me up and say, "Come over to my office and talk to me," and he asked me how things are going in biology, and I would tell him. And then he would say, "I think you should travel more." And so I went to the University of Chicago and worked one summer. And then they offered me a job, and I thought I'd like to go to Chicago because they had very good facilities. And Dr. Millikan told me, "Oh, no, you don't want to go to Chicago. I've tried that and it's just not a good place to be. You won't like it. Go there and try it; don't let them pay you anything. We'll pay you. You go there and try Chicago out; I bet you won't like it and will come back." So I went there for about six or eight months and tried teaching and doing research at Chicago. And Dr. Millikan was absolutely right: I hated it. So I just came back to Caltech. Experience is a great thing. And Dr. Millikan was very good at not forcing it on you, but letting you have enough rope to get your experience yourself.

I had another very interesting experience with Dr. Millikan, also, who was extremely good to me. He called me up one day and said, "Come and talk to me." And then he said, "Are you really traveling enough? You know, here in Pasadena we're very isolated from the rest of the United States, let alone the rest of the world, and you want to be sure to go to enough meetings." I said, "Well, I try to go to one national meeting a year." And he said, "That's not enough." He said, "I will arrange for you to have a special fund, a fund which you can draw for travel so that you could go to as many meetings as you want." And so he went to Mrs. Kerckhoff, the widow of the Kerckhoff that endowed and built the two units of the Kerckhoff building--by 1938, the second unit had been made; I forgot to talk about that. So, Mrs. Kerckhoff established the Bonner Travel Endowment. I never knew how much was in it. All I knew was that whenever I wanted to go somewhere, I could draw on this endowment, which apparently was bottomless, and get the money to go anywhere I wanted. So I traveled to a lot of meetings and had a good time and became very well known in the world of biology at a very young age. I got my degree when I was twenty-three, and I came back to teach when I was twenty-five; that's something that's pretty hard to do nowadays. My son has just become an assistant professor at the University of Indiana, after doing the same things that I did, except he spent more years as a graduate student. And he's thirty years old.

Berry: What field?

Bonner: Oh, my son is a molecular biologist who works on chromosomes-exactly the same thing that I work on. His name is James Jose Bonner-he's named after me and after my former landlord, José Planas, who lived at 290 South Michigan Avenue and was friend and mentor of many Caltech people. He was a gifted auto mechanic and ran his business in the backyard of 290 South Michigan.

Begin Tape 2, Side 1

Bonner: I was talking about the informality. Just a couple of more examples while we're on the subject. I was an associate professor, made an associate professor in 1943. And Dr. Millikan told me that I would be promoted to be a full professor in 1946. Of course, this was not written down: he just told me. In July 1946, George Wells Beadle was appointed chairman of the biology division to succeed Dr. Morgan. He came, and, of course, I already knew him. So I told him that Dr. Millikan had told me that I was going to be promoted to be a full professor, and it was his duty to honor this commitment. And so he said, "Well, we'll have to see about that." Anyway, he went over and asked Dr. Millikan whether it was true that he told me that I was going to be a full professor in 1946. Dr. Millikan said, "Of course I told him that; that's right. So you do it." And so I was promoted to be a full professor in 1946, which was not an especially young age; I was thirty-five years old. I never had any written commitment from Caltech until after Lee DuBridge became president and started making things more businesslike. Of course, in the meantime, the Second World War had occurred, and the Institute had had to become more businesslike because it had government grants and contracts. Before the Second World War, we ran completely on endowments and gifts and money supplied by the Rockefeller Foundation--at least, so far as biology is concerned.

Berry: Were you involved in any war work?

Bonner: Yes, I'll go back to that. But anyway, some time about 1950 or thereabouts, the dean of the faculty, Earnest Watson--the Watson who used to give the Physics 1 lectures--came to me and said, "So far as I can determine, you now have tenure." And the next thing I knew was that I had a letter from Lee DuBridge, saying that I was a tenured full professor, and that my salary would be so-and-so much, and so forth. So that was the first piece of paper I had that said anything relevant concerning my contractual relations to Caltech. And that was after being here twentyone years.

Berry: Was there any retirement plan then?

Bonner: Yes, the Institute had TIAA [Teachers Insurance and Annuity Assoc.], and I started that as soon as I became an instructor.

Okay, now we need to go back to the Second World War. Since I was primarily a plant biologist and plant geneticist, I began to worry about the state of the world in 1938. I wondered about what plant biology could do in case of a war and in case the war involved Japan--as it looked like it would. Professor Went thought similar thoughts. He had lived and worked in Java and knew that all U.S. rubber came from Southeast Asia. We thought about the fact that there's a plant that lives in Texas and northern Mexico called guayule, which produces rubber. And there was actually a company called the Intercontinental Rubber Company, which had been producing rubber in the United States from guayule for many years. In fact, up to 1910 most of the rubber used in the United States did come from the Intercontinental Rubber Company's operations with guayule. The Intercontinental Rubber Company had a large plantation at Salinas, California, and a large experiment station, mostly concerned with breeding. So we made an appointment with the president, Mr. Carnahan, and went up there to see him and made a contractual arrangement between Caltech and the Intercontinental Rubber Company to work on the physiology of rubber formation in guayule and what could be done to improve rubber yields by this plant.

After the beginning of the Second World War, after the involvement of Japan in the Second World War, our rubber supplies were suddenly cut off just as Frits Went had predicted. They had all come from Southeast Asia, from Indonesia and Malaysia. So the U.S. Government formed the Emergency Rubber Project. The Emergency Rubber Project did several things, but the main operation was to grow guayule on a very massive scale and extract rubber from it with the methods which had been developed by the Intercontinental Rubber Company (the Intercontinental Rubber Company was bought out by the U.S. government). The operation of the Emergency Rubber Project was turned over to the U.S. Forest Service. I was made an employee, a special non-civil service employee called an agent of the U.S. Forest Service, which offered all sorts of perks like Forest Service pickup trucks to drive around in. Caltech became a major national center for guayule research and development. I also had projects going on in Salinas and went there frequently. And I had projects going on in the desert, at the Bell Ranch near Indio, to determine the productivity of guayule in desert climates. I was asked by the Forest Service, by the director of the Emergency Rubber Project, a certain Colonel Roberts, to set up a planting in Arizona (Yucca Valley in southern Arizona) in a very severe Sonoran-type desert, to find out whether guayule could survive under Sonoran desert conditions without irrigation. It can't; and we established this quite firmly. I'm amused that now there is a resurgence in interest in guayule and a lot of talk about the government spending \$30 million to establish guayule as a commercial rubber,

producible in the U.S. It's talked about as a desert plant that can be grown in deserts without irrigation. We all know from the Emergency Rubber Project that it has to be grown with irrigation like any other crop plant. And the yields of rubber from guayule are miniscule compared with the yields from <u>Hevea brasiliensis</u>, the rubber tree of commerce, which I'll talk about later.

So I again did what Dr. Millikan told me. He said I'm not permitted to join the armed forces; I have to do what the National Defense Research Council says, and it says, you've got to go work for the Emergency Rubber Project. So I did. I imagine that I would have liked to have joined the armed services if I could have--because I have to wear glasses and have very poor vision, otherwise. But, in the first place, Dr. Millikan forbade it. And in the second place, I know in retrospect that what I really wanted to do was to get away from my unhappy marriage and just escape life by getting a new life. But actually, the work on rubber was pretty much of an escape anyway. After I'd worked on guayule for two years, they sent me to Mexico to work on another plant, called cryptostegia, which I rapidly showed was totally useless. And then I was sent to be the assistant manager of a rubber tree plantation in the very southern edge of Mexico-just far enough north so the South American leaf blight fungus didn't defoliate it. All of us were amateurs. There were two Americans running the plantation, and Mexicans tapping the trees to get rubber. It wasn't a very professional operation. But we made more rubber at that plantation than the whole Emergency Rubber Project did with guayule during the entire time that it existed.

I didn't permit myself to be idle while working on guayule, and I found out a lot of basic and interesting physiological properties of this plant--like the fact that it grows when it's warm, but doesn't make rubber. When the temperature cools off, it photosynthesizes, can't grow but turns all the photosynthate into rubber. So it has an alternating cycle, grow in the summer, make rubber in the winter--and has to grow in a climate where it doesn't get too cold in the winter so that it can do this. It's probably the most basic fact about guayule--that, and the fact that it needs water and is not truly a desert plant.

I mentioned parenthetically that there is a lot of renewed interest in guayule thirty years later. We had a meeting in 1975 in Tucson, called by the National Research Council. And all of the people from the Emergency Rubber Project who are still alive were brought back together to discuss what they'd found out, and the possibility of establishing a new Emergency Rubber Project with guayule. It was a really great reunion. I met there with people that I hadn't seen, some of them, for thirty-five years. It was just like an old home week, like alumni day at Caltech. But, as I said, nothing has come of guayule, and I don't think it will.

So that was my war work. I published a lot of papers on guayule and Cryptostegia and other aspects. The main thing that I learned about rubber that was interesting is the fact that no one knew or had any idea of the path by which carbon in $CO_{_{\rm O}}$ is fixed in photosynthesis and transformed into the isoprine molecule, which is the monomer of rubber. And therefore, beginning in 1948, I worked on this pathway and had completely mapped out the entire pathway, publishing the final nail in the coffin of the pathway in 1958. I then went around and gave talks on the pathway of rubber synthesis in plants. Actually, I did most of this work with Hevea. I showed that all rubber carbon atoms come from acetate and I determined all of the intermediate compounds in the conversion of isoprine to rubber. I went to Akron and gave a talk at the American Chemical Society's section there, and then gave talks at Firestone and Goodyear, which is the largest rubber user in the world. And I found out that there's nobody in the U.S. that's interested in the path of carbon in making rubber. But what I did get was an invitation to go to Malaysia in 1960, and that starts another phase of my life, which I will discuss later. My work on rubber did end up in something good. It ended up in an enormous amount of very interesting travel and some real, honest-to-God, good doing in developing countries.

In preparation for the Second World War, I did several things. One was I started early on this work on rubber, which got me committed to it, and it made it obvious to the NDRC that I should be assigned to work on that. The other thing I did was I bought a pick-up truck, because I had an intuitive feeling that there was going to be gasoline rationing and that trucks would be exempted. I bought a 1929 Model A Ford pick-up. And you know what? I turned out to be absolutely right [laughter]. I even drove Dr. Millikan around on his numerous trips in this pick-up truck, because it got gasoline and his car didn't. I had a car, too, but I had this pick-up truck, which got the gasoline tickets. That, and the Forest Service pick-ups really saved me. And the moral for today-and I should do it, but I haven't done it yet--is I should buy a pick-up truck again. Today, though, there's so many people have pick-up trucks for frivolous purposes that it may be that they won't get special exemptions.

After 1948, when I'd finished off all the guayule work and was working intermittently on the path of rubber, I decided to switch my field. I first decided this in connection with my first postdoctoral fellow, Sam Wildman, who had joined me during the war and worked on rubber also. And then after the war, we decided to develop what would now be called cell biology. We took leaves and ground them up and separated leaf cells into their component constituents. Leaf cells, most of them, contain chloroplasts, which are the agents that conduct photosynthesis and have all the chlorophyll. They also contain mitochondria, which oxidize sugars and produce ATP, which is the energy currency for the cell. And they contain smaller molecules, which are enzymes. We found out right away that leaves contain a protein which makes up about 50 percent of all the protein in the leaf, and which is a very large protein -- a molecular weight of about 500,000--easily detectable in the analytical ultra-centrifuge, to which protein we gave the name Fraction 1, and by this name it's still known. We subsequently showed, and other people showed as well, that this protein is the central enzyme of photosynthesis. It's the enzyme which joins CO₂ to a pre-existing five-carbon sugar to make two three-carbon compounds which are reduced by the reducing power generated in photosynthesis to make two three-carbon sugars from which the five-carbon sugars regenerated; and ultimately, after six rounds of this, a new six-carbon sugar molecule is generated also. Anyway, Fraction 1 protein was a great discovery, an important discovery. There's more of this protein in the world than there is of any other protein, by several orders of magnitude. It's been studied enormously, and I'm happy that I had an opportunity to participate in this discovery.

In the meantime, support for research became much more extensive than it had been earlier. Federal support was now suddenly widespread. I was supported by the Office of Naval Research, by the Office of the Quartermaster Corps, and then finally by the National Science Foundation, when it was formed, and by the National Institute of Health, which has been my main agency for financial support for the last twenty-five years. I also had a Frasch Foundation grant for twenty years, which is only \$10,000 per year (and I had to reapply for it every five years) but it was \$10,000 a year of absolutely private money, which was unaccountable to any government agency and could be used for all sorts of illegal things, like sending postdoctoral fellows abroad to meetings. Also, there was a vast rise in the number of postdoctoral fellowships available. When I got my fellowship to go to Europe in 1934, there were only twenty postdoctoral fellowships awarded in the United States. This number grew to thousands, so that it finally became the fashion that everyone had to have a postdoctoral fellows, and I had more graduate students. I've had a total of about a hundred graduate students that got their Ph.D.s with me over this period of time that I've been a professor. My first student got his Ph.D. in 1938, and my last student will get his Ph.D. in 1980.

So my laboratory began to grow, and I began to be able to work on several things at once. At this same juncture, I got a graduate student (1953) named Paul On Pong Tso. Paul came from Hong Kong. He'd gone to Ling Nan University in Canton, which is a Christian college where he had studied agriculture. Although his father was an Episcopalian minister in Hong Kong, in St. John's Cathedral (which is the Chinese Episcopalian church in Hong Kong and was at that time racially segregated; now it's everybody's cathedral), Paul wanted to be an agricultural missionary to mainland China. He had come to the U.S., after getting his bachelor's degree, to study horticulture at Michigan State, and he went to Michigan State because his uncle was head of the department of Oriental studies at that university. I went to Michigan State to give a seminar, and I met this funny, chunky little Chinese; and he told me he was going to be a graduate student at Caltech. And I said, "Well, apply, and we'll see." And he applied and was admitted. He came to be my graduate student.

A lot had happened to Paul. He'd decided that agriculture wasn't for him because it was too empirical; and horticulture wasn't for him because it was too empirical. He immersed himself in learning physical chemistry. And he found me isolating random entities from plant cells and finding out miscellaneous facts about how plant hormones do their work. One day Paul told me that he thought I ought to do more fundamental biological things instead of frittering around on the edges of science with these basically uninteresting observational phenomena. So I said, "Well, if you think that what I do is not basic enough, you can give us seminars every noon for the next three or four weeks until you can convince everybody in my group that we need to do more basic research." And he did convince us. And so you have to learn from the mouths of babes. I used to learn from postdocs, and then I learned to learn from graduate students; and now I'm learning to learn from undergraduates. Paul's remarks were very important, and they did change my course of research very rapidly. It's interesting because I'd already been rewarded in 1950 for my uninteresting work by being elected to the National Academy of Sciences. And I would have thought that I was on the right track, but clearly I wasn't. I've seen ever since that you have to change what you're doing from time to time in order to not become obsolete.

Berry: Were there one or two remarks that he made that were particularly . . . ?

Bonner: Well, he said that the work I was doing was just not basic biology.

Berry: Did he know anything about the work that you got into as a result?

Bonner: Oh, sure. So he convinced me that there were two things that were worth working on right then: One was to find out--there'd already been a little bit of work that indicated that there's a protein in the protoplasm which is responsible for the transduction of chemical energy into mechanical work. That's the protein that makes protoplasmic streaming; and a good place to study it is in the slime mold, <u>Physarum</u> <u>polyaphalum</u>. So we started out to study this, to find out what makes protoplasm streaming in Physarum. The upshot of it was that we isolated actomycin, which is basically identical to the actomycin in muscle, except that it occurs in a plant cell; and actomycin had never before been discovered in a plant cell. This actomycin is responsible for the transduction of chemical energy into the mechanical work which drives protoplasm streaming and also drives the movement of hyphae, which can

http://resolver.caltech.edu/CaltechOH:OH_Bonner J

Bonner-27

crawl across surfaces and also, we now know, causes chromosome movement. So that was a pretty basic and interesting piece of work, and it involved a lot of biophysical chemistry and electron microscopy and the characterization of the actin and the myosin that make up this nice complicated molecule.

The other thing that we switched to was to find out how proteins get made. And we found very shortly--and several other people found simultaneously--that proteins are made on particles which we now call ribosomes. Ribosomes are small particles about 250 angstroms in diameter, and they consist of two subunits--large and small subunits--and they're made of protein and RNA. We know today that the ribosomes bind to messenger RNA and translate the messenger RNA into protein molecules made out of amino acid monomer, which are fastened together into polymers--the information for the arranging of the twenty kinds of amino acids into the right kind of sequence to make the particular enzyme is contained in the messenger RNA which the ribosomes are decoding. But at that time, we didn't know about messenger RNA; we were only beginning to know about ribosomes. We isolated ribosomes and found out a great deal about ribosome structure and activity. They're essential in all protein synthesizing systems.

At this time, I had a postdoctoral fellow named Robert Holley. This was 1956 when we were well along with studying the physical structure and properties of ribosomes. It had already been shown that amino acids are converted by a special class of enzymes to amnioacyl enzyme complexes, a process which requires ATP. This is called activation of amino acids. And activated amino acids are the form in which amino acids take part in protein synthesis. Robert Holley, who had come from Cornell, showed that there's an entity in ground-up liver which takes the activated amino acid off of the activating amino acid enzyme and makes it into a new kind of complex. And he showed that this material is RNA. This is the RNA class now known as transfer RNA. Transfer RNA takes the activated amino acid, attaches it to the RNA, and it's the transfer RNA amino acid complex which is used for the assemblage of protein molecules. Bob Holley was so excited by his discovery, he said, "I'm going to work on this subject forever." He went back to Cornell, found out how to isolate transfer RNAs, found out how to isolate individual transfer RNAs, because there

must be at least twenty, one for each of the twenty amino acids. There are twenty different kinds of amino acids to be transferred (it turned out there are a lot more than twenty, because there's degeneracy; there are several different kinds of transfer RNAs for each amino acid). He isolated a particular transfer RNA in large quantities and found out how to sequence it and made the first sequence of a nucleic acid molecule. And for this, he got his Nobel Prize.

I decided at this time (1956) that the most important thing to do, the most important study left in biology, is to find out how RNA gets made. We already knew that the formation of RNA in a cell depends upon the presence of DNA. And the most obvious thought is that somehow or other the RNA gets made by copying the DNA, and that the RNA, which is a message for making a particular kind of enzyme molecule, is a copy of a sequence--let's say a sequence of the DNA, which is as long as a particular gene, and that the messenger RNA contains the information of a particular gene. So I decided to completely change my field, leave all other things aside, find out how RNA gets made, and find out about the control of gene expression--that is, what makes a particular gene be transcribable into RNA or not transcribable into RNA. And that will be the subject of a later tape, in a few moments.

I have already mentioned that I did a lot of teaching, and I did a certain amount of work on Caltech committees. I was very active with Chuck Newton in the formation of the Industrial Associates program beginning, I think, in 1950, and did a great deal of travel to industrial corporations to get them to become industrial associates. I once went on a ten-day mission with Lee DuBridge to recruit companies to the Industrial Associates. Of the many interesting things that happened on that expedition, I can quote you one--i.e. Lee (saying), "I hate this job." However, overall, it was a pretty successful job. We actually established an Industrial Associates office with a director; and from time to time, between directors, I acted as the acting director of the Industrial Associates office myself. We had a committee on relations with industry, of which I was chairman for many years. And this was a good thing too. I found out that as a result of my interaction with industry through the Industrial Associates, I got invited to be a consultant to various corporations. For example, I was a consultant for twenty years to the

Campbell Soup Company; consultant to Eli Lilly and Company; and a consultant to Smith Kline; and a consultant to IBM; and a consultant to Du Pont; and a consultant to Dow. And most importantly, after my initial visit to Malaysia in 1960, I was asked to become a consultant to the Rubber Research Institute of Malaysia, which is the richest and best-equipped research institute in Southeast Asia.

Begin Tape 2, Side 2

Bonner: I was a consultant to the Malaysian Rubber Research Institute until 1975. At that time I was asked to become a member of the Malaysian Rubber Research and Development Board, which is the board which determines what kind of research shall be done and what kinds of activities shall be carried out. Rubber research and rubber publicity and all things related to rubber are financed in Malaysia by an export tax on rubber. And this money amounts to a considerable amount; it supports a very large research program. I'm still very active in the Malaysia Rubber Research and Development Board, and go each year to Malaysia -- once or twice. We generally have a board meeting in London once a year also. So this is what I meant a while ago about how it's led to all kinds of trips. After a meeting in Malaysia (and the Malaysian government pays for my wife Ingelore to go also), we go to Indonesia or Borneo or New Guinea, or somewhere in the Philippines or Australia or Thailand; the whole of Southeast Asia is opened up to us once you get to Kuala Lumpur, paid for. And the rest of it, of course, you have to pay for yourself, but that's minor. Our trips to London have permitted us to do all kinds of interesting things, like travel to Europe, although Europe is not very interesting to travel in, because it's all like the U.S. now and in any case both of us have lived in Europe for long periods.

Another miscellaneous fact, which we skipped over and which was to do with the Industrial Associates, is the fact that in the middle 1950s it became perfectly clear to me that when I go, or any other faculty member goes, to an industrial corporation to talk about joining the Industrial Associates or to do consulting, the people one talks to are the people in research, and you don't get to talk to the people at the top of the managerial heap, who actually have decision-making power.

Bonner-30

I've tried to think of what kind of activity we could instigate that would get us right to the top.

One way which was opened up by Lee DuBridge was the one I referred to earlier. He asked me to go with him several times on trips to meet with the presidents or chief executive officers of corporations to try to get them to give gifts to Caltech. These trips didn't actually result in the raising of very much money, although they may in the long run have created some useful relationships with industrial corporations. Certainly our visit to IBM did: It started Caltech's long-time relation with IBM. I'll never forget that visit to IBM. We had a date to see Thomas J. Watson, Sr.

Berry: Who was with you?

Bonner: Lee DuBridge.

Berry: I see, just the two of you, and this is in New York?

Bonner: Yes. So there he is sitting at his desk, this strong-willed, testy, crusty old man, surrounded by signs that say, "Think." So Lee DuBridge and I started discussing how computational activity is something that Caltech is interested in and has a start in, and it would be good for us to make connections with IBM and support them. And Lee asked some substantive question--I've forgotten what it was--which required a technically informed answer, which Thomas J. Watson, Sr., couldn't provide. So he said, "I can't answer that right now; I'll have to call my son." So he called in Thomas J. Watson, Jr.; that's the Watson we know. And Thomas J. Watson, Jr., came in the room and he said, "Hello, father." And then the father asked Thomas J. Watson, Jr., something; and it was "Yes, Father, no Father; yes, Father, I'll do that right away." I couldn't imagine how this guy who was so subservient to his father would ever be able, when the time came, to take over the running of that giant multinational corporation. But you know what? He did. And he did just fine. Amazing. He really had a good upbringing. But he was certainly servile to his father.

Berry: I've been reading about his father in a book on the history of computers. His father was quite a salesman, wasn't he?

Bonner: Yes. And of course, Thomas J. Watson, Jr., considers himself to be a master psychologist now, not technical at all. Interesting. Well, anyway, what came out of that was we got our computing center.

Berry: I know Caltech really got into that fast. And that was the start of it.

Bonner: Yes. And they of course gave us all the computers and everything. They gave us the money for the building, gave us the computers.

Berry: Caltech was to do what? Research on computers to advance. . . ?

Bonner: Yes, and that was to be a showplace for IBM. And they were ultimately stopped from giving us computers because the Federal Trade Commission said it was unfair competition. So they gave us money instead--\$5 million a year for years and years. Maybe they still give it, I don't know.

Anyway, to answer the question which I'd posed, there's a second way which I actually thought up in consultation with the then-director of the Industrial Associates. Our first director, Bob Bartz, whom we stole from MIT, and I thought about how to get closer to the top. Then Harrison Brown and I decided to organize a lecture which would last a whole day, and which would take a look at the future of technological society--the future of resources, the future of energy, the future of population, the future of what we're going to do with the developing countries; and are there enough brains in the world to run this more complicated society; how complicated can it get? So we organized this and we entitled this one-day seminar, "The Next Hundred Years" -- a look at the probable developments during the next hundred years. We gave this one-day-long presentation to the boards of directors of more than fifty of the leading U.S. corporations. Harrison and I were really amazed at the difference in ways of operations of different corporations. We thought of writing a book on the ethnology of boards of directors and the comparison of their

different methods of operation and, in some cases, extreme, rigid stratification. In some companies (like Texaco for example), this was contrasted with the extreme looseness of organization where anybody can talk to anybody, as in the case of Shell. In some organizations, only the board chairman can ask questions of the president, and nobody can ask a question of the chairman. But in Shell, they actually had young people in as directors. There was one guy about twenty-five years old. And he was there specifically to debate with people--a smart kid--and anybody could ask any question; it was totally open and free discussion. We decided that if we wrote a book comparing the modes of operation of different boards of directors, that would be a book you could only write once; you'd never get back in again.

Anyway, it's been generally acclaimed that this enterprise, which took us about a year to make all these visits, did have a major impact in bettering the relations between Caltech and industry, and making them take us more seriously. It did have a great impact.

Berry: Now this one, "The Next Hundred Years," wound up as a several-day symposium here, didn't it?

Bonner: It ended up--the last one, the last presentation, was a presentation on the Caltech campus for all the local companies that we couldn't visit individually, especially aircraft and electronics. And I think maybe it was two days. The book, The Next Hundred Years, came out of this traveling circus. Harrison and I decided later (the book came out in 1957), in 1967, to have another symposium on campus to look at our projections ten years later. We invited other people besides us to participate in that, and that resulted in this report called The Next Ninety Years. The Next Ninety Years was more informal. And then we had The Next Eighty Years in 1977; that was informal also. But it's interesting that many of the predictions that we made, we were right on the button--like when the U.S. oil would start to disappear, exactly the right year; and when the world oil would top off and start to disappear -- we were just about on target there, too. We may have been a little bit too generous. The disappearance of the Iranian oil is screwing us up a little bit. But we're just about on target on that, too. But some of the things we were absolutely wrong on

were: we never imagined in our wildest dreams that Arabs could ever get together to agree on anything like OPEC. Also, we were too optimistic in thinking that developing countries could develop. And, of course, because of the interest that I developed in the developing countries through this exercise, I've had a lot of opportunities to go to developing countries and to study them and to begin to understand much more deeply why they're not developed already. There are always good reasons for it. And these reasons are summed up in <u>The Next Eighty Years</u>--my new knowledge. I've begun to see that in a developed country, you can't look at them as a country; it's a whole bunch of strata of society. In a developing country there's a thin narrow strata of society that has all the wealth and all the power, and they're all crooks. And everybody else is poor and they're kept that way--that's the way societies organize. In what we call a rich country it's different. The wealth is distributed much more broadly.

Berry: A lot of the undeveloped countries are undeveloped because they are purposely kept back by a small, wealthy, powerful class.

Bonner: A clique, yes. Nigeria is a very good example. Nigeria is a very rich country--it has great big oil supplies which it sells for an enormous price. None of that oil income has ever gone into any public development; it's all gone into private bank accounts of a few generals. Terrible corruption.

Berry: People don't rise up.

Bonner: Well, the people don't have any power. You see, the generals own the army. This is another secret: you've got to own the force. But all these things aren't clear to the regular humanitarian who wants to go out in the world and do good.

Berry: I guess not. The Peace Corps people who do, do some good but I guess . . .

Bonner: They do good but on a very small scale, all below the corruption level. So that's been another of my incarnations.

Berry: You really have a whale of a background, because I noticed the places you've been--there's hardly any part of the world that you haven't been.

Bonner: Well, I've only been in Egypt one night. So I'm curing that: on the 28th I'm going to Egypt for two weeks. I've just been employed by the University of Alexandria as a consultant.

Berry: Have you? In what field would this be?

Bonner: On the organization of their scientific research program, like going every year for some number of years. Ingelore won't go with me; she says I've traveled too much this year already. You see, we were more than two months in China.

Berry: That description of China that you wrote was just wonderful.

Bonner: Then I had to go back to Malaysia again after that. Then we went skiing for two weeks after that. And then our daughter got married in Cambridge, and we had to go to that. Ingelore is exhausted. She doesn't want to see an airplane.

Berry: You thrive on it.

Bonner: Well, the difference is I can sleep on airplanes. She can't. I got to know an awful lot about agriculture through this travel, too. I didn't really talk about that. Because of the fact that I had become somewhat known as an all around plant biologist and because I wrote a book on plant biochemistry which had a very important impact, I became known as an agricultural specialist.

Berry: What's the title of that?

Bonner: <u>Plant Biochemistry</u>. It's now in its third edition. I was asked to go to the Commonwealth Agricultural Conference in 1949; they have one every five years, and this one was in Australia. So I went by Pan-American to Australia. I had those reclining seats with the footstools like they're advertising for first class. They had them in 1949--the whole airplane, every seat had them. It's been all downhill since then. It was a DC-4, however, and it took days to get there. It went very slowly. We landed at Canton Island, which is basically just a landing strip, to refuel. I got an enormous insight into the agriculture of Australia. As a result of that, I got appointed as consultant to the Commonwealth Bank of Australia on how to use the local Australian resources for development of agriculture and industry in Australia, and also, the development of education. I made a report on higher education, which was adopted. They were trying to halt the flow of people who graduated from undergraduate school who would all go to England, get their graduate degrees, and never come back. This was because they had sort of a Russian system: research institutes in the Commonwealth Scientific and Industrial Research Organization where all the research is done, and the universities are just teaching institutions. And I made a report to show how easy it would be to incorporate the CSIR laboratories as the graduate departments of universities, which they then did. And it really worked like a charm. Now there's lots of good graduate education in Australia. The Australians come here as postdocs, not as graduate students.

Berry: So they stay.

Bonner: So now they stay. And it's partly responsible, I think, for the very rapid industrial and scientific buildup in Australia. So I stayed there doing that until 1962. And in 1962, the then-prime minister, Menzies, offered me a job. He wanted me to go become an Australian citizen and stay there and take over the direction of a large part of the CSIRO. I had just started my work on the control of gene expression. I would have loved to have gone to Australia; it's a really nice place. It's as big as the U.S. and all like California. It's really neat. But then I would have had to become a full-time bureaucrat. And I just turned down being chairman of the biology division, because I didn't want to be a full-time bureaucrat.

Berry: I know you did turn that down here several times.

Bonner: Yes, I did. So I told Menzies that I wouldn't do it. So I was cut off from all of my consulting activities in Australia--never been invited back. However, luckily I was already hooked by Malaysia. JAMES F. BONNER Session 2 March 14, 1980

Begin Tape 3, Side 1

Bonner: We were talking yesterday a little bit about skiing. And I mentioned the fact that after my parents moved to Salt Lake City--the first winter we lived in Salt Lake--my parents gave me a pair of skis; I was six years old, and the skis were about four feet long. So I took up skiing and that was the natural thing to do because Salt Lake has got an enormous concentration of Scandinavians--Norwegians and Swedes. (In particular, they appear to be especially easy to convert to Mormondom, and so there's a lot of them there.) And they all were skiers. When I got to be I guess in high school, I actually got some ski lessons from Sverre Engen--one of the Engen family, which is a family of superskiers who run the ski school at Alta. In the first years of my skiing, we did things like just ski down hills as fast as we could. And we ski-jumped, and I got to be pretty good at ski-jumping. We played fox and hounds in the foothills of the Wasatch Mountains behind my parents' house.

And then skiing started to be invented. In the 1930s, the Arlberg method of skiing came from St. Anton in Austria. And we all had to learn how to do stem turns they're called, where you start out with a snowplow, then lift your inside foot up and bring it around parallel to your outside foot. This is a good way of turning. Then, in the early 1950s, the French school invented parallel skiing. It turns out that you can just keep your skis parallel and point your knees in the direction you want to go, and you go. It makes skiing enormously more fun. And then it turned out that you don't have to swing your shoulders around to turn: all you have to do is to turn your knees in the direction you want to go, unweight the uphill ski, and bend out away from the mountain, which is very unnatural -- because everybody wants to bend into the mountain -- but you bend out, and you turn just marvelously. Then the Austrians showed that you could just wiggle your fanny and turn, too. That's called So down through the years I've had to learn about every five years a new method of skiing. Now I think I'm stabilized.

After the Second World War, when skiing started to become fashionable in Southern California, the lines at the chairlifts started to become so great and I got so tired of waiting in line, that I joined the Ski Patrol, because ski patrolmen get to jump the line and get right on a chair and ride up. By 1950 I'd worked up to being a national ski patrolman, which is as high as you can get. I was a ski patrolman for almost thirty years. I've given it up now. I think the skiing public deserves younger ski patrolmen than me. But it really was a great thing while it lasted. I was a ski patrolman on Mount Waterman for years and years most of the time. And I was a weekend ski patrolman at Mammoth, and I was a ski patrolman at Alta from time to time. I still go skiing at least thirty days a year and try to get more than thirty days in. I used to get forty or fifty. It's a sport that increases in pleasure every year. This year skiing has been probably one of the most pleasurable seasons ever. I recommend it very strongly. By the way, I've been skiing now for almost sixty-four years, and I have never been hurt; I never broke anything or busted myself up or had anybody run into me or anything serious. I think being a ski patrolman is awfully good. It makes you be careful and look out for what's going on, and it teaches you how to ski safely in every kind of crud, and to avoid rocks and branches and stuff. People do lots of stupid things and get hurt. But if you're a ski patrolman, you learn to watch out for stupid things so you don't get hurt. I recommend ski patroling as a really wholesome sport.

It also has helped me in another way. During the years of child raising and all that, when you have to decide whether to stay home and do homework and help with the children or else go skiing, if you're a ski patrolman you can say, "Well, I should stay home and help with the work, but on the other hand, there are those people up there that depend on me, and it's a duty for me to go and be a ski patrolman." And in this way, you can make the work ethic work for you instead of against you. Going skiing is not a goof-off from duty--it <u>is</u> duty. And you look at it as a duty. And so it eases the conscience and makes skiing a positive good. It's a great example of the fact that man's ability to rationalize is infinite.

So much for skiing, I guess.

Oh! I helped found one of the first ski clubs in Australia while I was out there working for the Commonwealth Bank. We founded a ski club--Blue Cow Ski Club--which has a chalet on Blue Cow Mountain. We have a lift and a nice chalet there, where people can stay. I've been skiing almost every place in the world where there's skiing--like New Zealand, and Australia, and Switzerland, I've never been skiing in Canada, I guess, and all over the U.S., except that I have never been skiing in the East. And I have been assured by my son, Jose, who went to MIT, that the skiing in the eastern United States is an entirely different sport. They have these little icy slots down through the trees, and it's not like skiing on the wide open bowls of Utah, Colorado, and California.

Berry: Were you involved at all in interesting the students in any ski activities here?

Bonner: No, I have never been associated with the Caltech Ski Club, partly because my activities as a ski patrolman involves the obligation of going to a ski area and patroling. I have seen lots of Caltech students while skiing, and I've given ski lessons to lots of Caltech students, but not in connection with ski club duties. In fact, I this very year gave some skiing lessons to two Caltech students. Well, let's leave skiing.

I think we got to the fact that I started to work on ribosomes, and Bob Holley discovered transfer RNA--the transfer RNA of acyl amino acids. And now I guess we should go to the sixties.

In 1960, I made a policy decision that I would forego all previous work--like protein synthesis--to study the most interesting remaining part of biology (I thought at the time): namely, how does RNA get made in the first place? And as I said before, we thought that it got made somehow by copying DNA. So I set out with a new postdoctoral fellow, R. C. Huang, who's now a tenured professor at Johns Hopkins University, to see if we could find an enzyme that would catalyze the making of RNA, but dependent upon the presence of a DNA molecule. We almost immediately found this enzyme, which is now called RNA polimerage. It takes the four riboside triphosphate monomers and copies a DNA molecule to make an RNA

year, 1960, there were three other groups besides us that discovered RNA polimerage, so it was not a unique discovery; it was sort of in the air and a discovery ready to be made. We also discovered that if we isolate, not pure deproteinized DNA, but DNA as it occurs in the cells of higher organisms, the DNA is complexed with proteins; and the DNA complexed with proteins is a very much poorer template for the making of RNA than is deproteinized DNA. We found out that if you take these proteins off the DNA, DNA becomes a good template; and if you put the proteins back on it, it becomes a bad template. So obviously, those proteins are very interesting, because one could imagine right off that they somehow control the transcription of RNA. And at this same time, in 1961, it was shown that the RNA copied from DNA is in fact really copied by ribosomes to produce proteins. One could guess that the RNA transcribed from DNA is a way in which information is transferred from genes to the final gene products-enzyme molecules. So I set out to study these proteins; those that are complexed with DNA in the chromosomes of higher organisms. They belong to a class called histones. They had been discovered almost a hundred years before, but nothing of substance had been done to find out about how many kinds of histone molecules there are, and whether they are the same in different creatures or different in different creatures, and whether they're the same or different in different organs of the same creature.

So not knowing exactly what way to turn, Paul Ts'o and I organized a conference, for which we got lots of support money; it used to be easy to get lots of money for conferences in those days. We got money from the Rockefeller Foundation and the National Science Foundation, and so forth. We brought to the conference, which was held at Rancho Santa Fe near San Diego--a nice isolated place that is hard to escape from--we got about forty people. We had every person in the world that had done any significant work on histones. And it was called the "First World Conference on Histone Biology and Chemistry." I've been asked many times why I didn't have a follow-up conference, and I've always answered that by saying, "You can't have a second First World Conference on Histone Biology and Chemistry." So that's the reason why we didn't have another one: you can't have a second first. The take-home lesson from this conference was that there was nobody in the world that was doing any

sensible chemical, or making any sensible chemical contribution to the study of histone chemistry and/or enzymology. It was clear, therefore, that we would have to grow our own new experts.

Luckily, 1963 coincided with the coming to Caltech as a graduate student a young man named Douglas Fambrough, who came from the University of North Carolina. We sent Doug Fambrough to spend a month at Stanford, where Kenneth Murray, who was a postdoctoral fellow in the laboratory of J. Murray Luck at Stanford, had found a method of separating histones into three classes by column chromotography. So Doug went there and learned everything that Kenneth Murray had to teach him and came back. And we set up our own laboratory for the study of histone chemistry. We also made an important advance in methodology. Doug Fambrough applied the newly invented, so-called disc electrophonesis to the separation of histones from one another; and particularly, used disc electrophoresis for the determination of the purity of histone fractions. The combination of this new disc electrophoresis and column chromotography made it clear within a few months that there are five classes of histones, and that these five classes, all very similar to one another, are found in widely dissimilar creatures-creatures as dissimilar as plants and cows. It became very obvious right away that the histones of different organs in the same creature are the same. The same five histones are found in all the different kinds of cells, specialized cells, in the different organs of a higher creature. We also found that it was quite easy to isolate pure histones separated from one another. We isolated massive amounts -two grams--of the smallest of the histones--a histone of about 10,000 molecular weight. We isolated two grams of it from a plant, pea seedlings, and two grams of it from a cow, calf thymus glands. We called upon the help of my colleague, Emil Smith and his postdoctoral fellow, Bob Delange at UCLA, who were experts in amino acid sequencing, to amino acid sequence this smallest, and therefore simplest, of the histones.

To our amazement, it turned out that the amino acids sequences of these two histones were basically identical. This means, of course, that the gene for making histones had been established by the time of the common ancestor of peas and cows, which must have been at least 600 million or more years ago; and that means that that's a very conserved gene, that every amino acid in the histone molecule has a special function, and that

the mutation and alteration of histones by mutation is therefore forbidden in evolution. Therefore the histones must play a really important role. We found out other interesting things, such as the fact that histones have an amino end full of basic groups that bind to the phosphate groups of DNA; and a hydrophobic end, through which histones bind to one another. We also found that the five kinds of histones are present in a special stoichiometry. For each one molecule of histone 1, there are two molecules of histone H_oA, two of histone H_oB, two of histone 3, and two of histone 4. We sequenced histone 3 also. But, of course, it quickly turned out that the conservation of amino acid sequence in histone molecules is very interesting. In Nature, a "News and Views" article about histones concerning our discovery, which was published in 1968 about histone 4, said that, "This is the first evidence that histones constitute anything other than glue." This brought a lot of general interest, and it turned out the world is full of people that know how to amino acid sequence proteins but don't have anything to do. So the sequencing of histone molecules became a growth industry all over the world--done in England, France, Spain, South Africa, Japan, and the United States, and probably I have left out one or two countries where it's been done also. Anyway, we gave it up. Every histone has been sequenced from at least two creatures now, and we know everything that is interesting to know about histone sequences.

I've made a big jump from starting to work on the transcription of RNA from chromatin and the study of chromatin to the final establishment of the sequence of histones. We discuss it in five minutes, but it all took eight years. And I've left out a couple of interesting things that happened during those eight years.

In 1961, in company with Bob Bandursky, who'd been formerly a postdoctoral fellow with me and was a professor at Michigan State University; Richard Schuster, a Caltech graduate who was one of my fellow ski patrolmen; and Jacob B. Biale, a professor of biology at UCLA, we jointly organized an expedition to Nepal to go mountain climbing in the Himalayas. The occasion was that there was a biochemical congress in Moscow, and three of us were sent by the U.S. government to this conference. The U.S. had committed itself to saturating the conference with Americans to show how much better we were than the Russians in biochemistry. And I think at least two-thirds of the attendees were Americans. Richard Schuster, who isn't a biochemist, had to go on his own. But luckily, the company he worked for had a factory in France, so at least he got his fare paid to France. It turned out, though, when you get to Moscow from Pasadena, you're halfway around the world, so it doesn't cost any more to come back by Nepal and Japan. So we went to the biochemistry congress; then to Soviet Central Asia; then to Delhi; then to Nepal, where, to our amazement, we found that all the climbing gear that we'd air freighted there was actually there. We had a one-month safari with two Sherpas and eight porters, and made an attempt--which did not succeed-on Annapurna IV in West Nepal. It was an absolutely stupendous trip, and one that I will forever remember--a lot of danger, a lot of interest, a lot of beautiful mountains. It's documented in stories which I've already written and which are published and further documented in my pictures.

Berry: Wasn't there something that you were asked to bring back from a yak?

Bonner: Oh, yes. My brother Walter, who's a professor of biophysics at the University of Pennsylvania, is what he calls a comparative coprologist: that is, he collects the dung of different creatures. And he wanted me to bring him back some yak dung, which is unavailable in the United States, because yaks live only at high elevation and they live mostly in Central Asia. A lot of them live in Nepal. They're domesticated creatures, and they serve as beasts of burden, and they serve as food, and they serve as animals that can be milked, and they're all-around, all-duty creatures. Well, unluckily, it turned out that, in the high mountain meadows, each yak is followed around by a little child who picks up the yak dung right away and smears it on the wall of the yurt, which is a felt tent in which the Tibetan natives live; and it's dried and used for making a fire; so to get fresh yak dung is pretty hard. One morning I talked to a local Tibetan yak herder, and made indecent motions; I pointed at the yak and I made indecent motions to my own rear and to the yak's rear and pointed at me that I wanted to get something from the yak. All of a sudden, a great light dawned, and the peasant went off and he came back in about twenty minutes with two yak tails. Luckily for my brother, the comparative coprologist, the yak tails were pretty well saturated with yak dung. So I

gave him one. I still have one myself that's sitting in my office; and people ask me, what's that? And I say, "That's my yak tail." And the other one is hanging in the foyer of the Johnson Foundation, which belongs to the biophysics department of the University of Pennsylvania. That's the story of the yak tail.

After this wonderful trip, I and Dick Schuster and Bob Bandurski went on around the world. We went to Burma, thence to Hong Kong, thence to Taipei, where I gave some lectues; then to Japan where I went on a long lecture tour; and thence home. Once you've been around the world in one direction, I figured --- I've taken enough physics so I know that when you have an unpaired spin you should try to get it paired again. So the next year I took a trip and went around the world in the other direction. This was also a wonderful trip. I started out by going to a meeting in Australia. This was the one where I was told by the prime minister, Mr. [Robert Gordon] Menzies, that I had to become an Australian; and I said I wouldn't. So he cut me off of his list, and I had to quit being a consultant to Australia. I continued, had a marvelous ski trip in Australia, and gave some talks, and attended a meeting, which was the consecration of the new Australian phytotron in Canberra, then took the plane to Perth on the west coast of Australia. I then took a flight that goes once every two weeks from Perth to Johannesburg. It turned out that the captain of the Qantas flight was a guy that I'd been skiing with the week before in the Snowy Mountains, except that he didn't know that I was going to Johannesburg. And I didn't know that he was a captain of Qantas. So it all worked out very neatly. He let me sit in the cockpit, and I found out a lot about flying across the Indian Ocean. There's no radio navigational aids, and it's all done by old-fashioned shooting the stars and the sun. The navigator took a reading every fifteen minutes. There were two crews. And when we finally got to Mauritius, where it stopped to refuel, we were less than fifty miles off course. And this was after almost twenty-four hours of flying. It was a Lockheed Constellation, specially fitted up to take only thirty-five passengers, and the rest of the passenger compartment was for gasoline. It could go almost forever. It landed in Mauritius, and the reason they used the Constellation in 1962 was that the runway in Mauritius was not long enough to accommodate a 707. We stayed for a day in Mauritius because the crews had to rest up. Both

crews had done the total amount of flying that they were permitted to do without twenty-four hours' rest.

Berry: Prepeller plane?

Bonner: Yes. (A Constellation!) And I can tell you that when you cross the Indian Ocean across the middle of it like that, you don't see anything; there's nothing down there.

Then we went to Johannesburg, and I took a long trip through East Africa to see the animals. I went to Kruger National Park for ten days; then up through Rhodesia and Zambia; and to Victoria Falls. Went on a trip up the upper Zambezi River. It turned out that I went down to the boat dock to get on a boat to go on up the upper Zambezi River, and the boat and the Zambezi River looked exactly like the jungle ride in Disneyland; I need not have gone. It was exactly the same. And the river was all full of crocodiles opening their mouths and shutting them; and hippopatami, with their heads sticking out; and monkeys in the trees--it was just Disneyland revisited. Then I went up to Kenya and saw a lot more animals. And then I went to Addis Ababa, and Asmara. Beautiful country. No wonder people are fighting over it now. Then on to Cairo. And then from Cairo to Pasadena in one day. So I got my spin paired--around the world completely, once in each direction. That was 1962.

Well, as I think I mentioned before, I'd been teaching Biology 1 for many, many years. So in order to get out of it, I accepted a job of being Eastman Visiting Professor at Oxford. So in the summer of 1963, I went to Oxford. It was a condition of the NIH continuing my research grant that I return every six weeks or so to Pasadena to supervise things. In the meantime, Jerry Vinograd, my colleague, agreed to take over the official supervision of my research program. I revisited Caltech every six weeks. And it turned out that, although the Eastman Foundation gave me \$5,000 for travel expenses, I didn't use any of it, because every time I wanted to come back to Caltech, there was some other reason for coming--like the dedication of the computing center, at which I had to give a talk. Another one was I came to go on a site visit nearby for NIH, and such like things. Each trip paid for itself, and I had the \$5,000 left over. This was a really money-making proposition. Add to that the fact that I

spent my one year at Oxford and gave my eighteen lectures on molecular biology, which were the only ones in molecular biology given at Oxford at that time, added to the fact that I had an awful lot of fun. And in addition to all that, Caltech paid the difference in salary between what I was paid at Oxford and what I was paid at Caltech. And the next year, it was decided that Oxford and Cambridge professors were underpaid, and they got a 25 percent raise; and they paid me retroactively a 25 percent raise [laughter]. It was a great success. Everybody had told me how great it is to take a year off and go somewhere else--it's a great thing. And you know what? They were right. I wrote a book, called the Molecular Biology of Development, and I made the second edition of Plant Biochemistry. I did a lot of laboratory work. And I had two very good graduate students; one of them came back from Oxford and finished his work at Caltech, and the other one stayed at Oxford. The work of the one that started with me is what he got his Ph.D. on; and he is now a professor in the U.S. I've never been back to Oxford since. It was a lot of fun, though.

Nineteen sixty-seven, which we've skipped also, was the year, of course, of <u>The Next Ninety Years</u>-that is, <u>The Next Hundred Years</u> looked at ten years later.

Well, in 1968 histone chemistry was pretty well finished up. So I went on to try to find other ways in which the control of gene expression could be studied. It was clear that the histones don't hold the secret of the control of gene expression because histones don't bind sequence specifically; they can't tell what gene they're binding to. There are the same histones in every cell, and all the DNA is covered with histones. So there must be something more subtle. The key to this was really discovered in '68 and '69 by Keiji Marushigi, who was a postdoctoral fellow from Japan, who was stayed in the U.S. and has become a U.S. citizen. He and his wife are both biochemists, and they are extremely capable people.

Berry: Is that here?

Bonner: Yes, at Caltech. He's now a professor at Ohio State. I think he deserves to be in a better place than Ohio State. But Marushigi in his usual quiet way of finding something absolutely unusual and totally

unexpected, showed all at once that the transcribed portion of the chromatin of a cell is very much more sensitive to attack by nuclease -that is, enzymes which chop up DNA--than is the nontranscribed, the inactive portion of chromatin. And by very gentle treatment with nuclease, it's possible to separate the transcribed DNA from the nontranscribed DNA. In this way, Marushigi showed that the nontranscribed portion has histones on it, but the histones are in some sort of different confirmation than they are on the nontranscribed chromatin. And this opened up the whole field of finding out what this difference in structure is. And it's turned out, of course, that in the nontranscribed portions of chromatin, the histones of classes 2-A, 2-B, 3, and 4, are bound together into an octameric unit by their hydrophobic tails. The DNA is wound around each of these octanemic beads twice, to form a bead, which is connected by a spacer to the next bead. And on the spacer, histone 1 is bound. In transcribed chromatin, the beads disappear, and the histones are strung out along the DNA. The DNA relaxes into full-length, or nearly fulllength, DNA not wound around anything. And because it's an extended confirmation, most DNA of the transcribed chromatin is accessible to nuclease as well as to other enzymes, as RNA polymerase, so that it can be transcribed.

We showed that the DNA isolated from the chromatin by nuclease attack in this way is a subset of one of the genes grown in liver. Ten percent of the genetic complexity is released as active chromatin--that is, active chromatin in the sense that it can be transcribed. Thus by every measure, the transcribed chromatin is actually the transcribed fraction of the genome. This work only identified the transcribed portion of the genome, it didn't tell us why or what it is that makes it different from the nontranscribed portion of the chromatin. We very quickly found out what it is that makes it different. It is that in the transcribed portion of the chromatin, the histone molecules are acetylated. The terminal amino groups, the so-called epsilon amino groups of the lysine molecules of the histones, interact with acetyl groups which makes acetyl lysine which is not charged, so that these N terminal peptides of the inner histones can't bind to DNA. They let go of their grip on DNA, and the DNA becomes uncoiled from the bead, the so-called nucleosome, and becomes extended. We then isolated the enzyme which acetylates chromatin. This enzyme also

is non-sequence specific: it will acetylate the histones on any sequence of DNA. So there's still some element in the chromatin which tells the acetylase the histones of which DNA sequences it's supposed to acetylate and make into active genes. We have a new approach to that, which I'm going to discuss in a moment.

In the meantime, many other things had been happening. I'd been going to world conferences all over the place. We had a wonderful trip in 1971, starting at the Argentine Biochemical Society meeting in San Carlos de Bariloche, about a thousand miles southwest of Buenos Aires in Patagonia--marvelous place, beautiful place. I'd really like to go back there. And we went from Patagonia back to Buenos Aires, and went to Rio. And from Rio, we went to Dakar. And from Dakar we went to Lagos, Nigeria.

From Lagos, we went to Kano. I'd always wanted to go to Kano. It's a very historic place, a seat of Moslem culture a thousand years ago; a medieval town, a medieval market town at the end of one of the caravan routes from the Mediterranean, across the Sahara to sub-Saharan Africa. They still have a camel market every Friday morning. And they even have a sewage system that consists of open ditches. It's just an absolutely marvelous old city and incredibly interesting. We visited it and met a lot of interesting Nigerians and talked to a lot of people, and generally had a great time. From there we went to the Ivory Coast and Niger and Upper Volta, and thence to Timbuktu and Mali. Timbuktu is a very, very isolated place, also on the edge of the Sahara, and also a medieval city, founded about 1025. Timbuktu means "the market of the old woman," and it was actually started by an old woman who set up a trading post. And again, it's the end of a trade route from the Mediterranean to sub-Saharan Africa. Timbuktu is not far from the Niger River; and the salt and other goods brought from the Sahara are transferred from camels in Timbuktu to boats, which go down the Niger River to Nigeria. And they're still doing that today. It's a Tuareg city; it's not a Negro city. The Tuaregs are bedouins. The men wear the veil, and the women don't. They're Moslems, but they were converted to Islam in 1400. Each Tuareg was given the choice by the Arabs of either converting to Islam and getting an extra wife given to them, or else being killed; so most of them took the first choice. They wear blue robes dyed with indigo, and indigo comes off on

their skin, so they're often called the "blue people." And generally, they have a miserable life. They bake bread all day long, and the bread is baked in outdoor ovens. The bread is interesting because it smells so good and it looks so nice, and you bite into it and discover that what you thought was all flour and raised dough is actually half sand because the wind is blowing all the time, and the bread, cooked outdoors in these outdoor ovens, is just full of sand.

Anyway, that was an immensely interesting trip. We took lessons in camel driving; and we had use of the land rover, and got far out into the Sahara to little Tuareg villages and to other interesting places. We went from there to Las Palmas, and from there to Marrakesh; nobody should go through life without visiting Marrakesh. It is perhaps one of the most interesting cities in the entire world. Again, a very ancient medieval city.

Berry: Is it on the Sahara?

Bonner: No, it's north of the Sahara. It's at the foot of the Atlas Mountains. And you have to go around the Atlas Mountains to get at the Sahara; it's in the fertile northern plains part. It's not deserty. It's interesting that the city itself is inhabited by Arabs, but all the mountainous parts are inhabited by Berbers. I hadn't appreciated before the clear-cut distinction between Arabs and Berbers. The Berbers are tall and very Caucasian looking, whereas the Arabs are generally shorter and squatter and more Semitic-looking. And the Berbers are always poorer, too [laughter]. The only Berbers that are rich are the ones that live in countries that have lots of oil; and that doesn't include Morocco.

From there, I went on to Rome to the yearly conference which Caltech had (a program initiated by Harrison Brown). We had for quite a number of years a program funded by the AID of the State Department, a program to study population growth and population problems and agricultural problems in developing countries, and to study this in a depth and detail which had never been used before. We had about twenty field workers, chosen from the AUFS*, which Caltech used to support but no longer does. We

*American Universities Field Service

had a yearly meeting of all these field workers in Rome, which was an excellent idea. We had a yearly trip to Rome at Christmastime. So this 1971 trip ended up in Rome.

But I can't go on talking about trips. I'm going to talk about one more trip and that's all; and I'm going to talk about that later.

Berry: You had interests outside of biology, and you published and spoke on several things outside of biology. You were talking about when we got into genetic lottery, test-tube babies.

Bonner: Yes. My interests in things outside of biology, which are actually inside biology--I think all of the matters which you just mentioned which have to do with population growth and human life and food production, etcetera, is part of biology, except it's a part that's generally left to the people who don't know anything about biology. So after my experience with <u>The Next Hundred Years</u>, I had a continuing interest in population problems and in agricultural problems. And it was in this role and because Harrison Brown, my colleague, was also getting an ever-increasing interest in these same problems, that we founded this program for the study of population growth, which was, as I said, financed extremely liberally by the State Department; it was through the State Department's support that I got to visit West Africa for the first time to make the studies that I did make.

My acquaintance with many different cultures, all the way from-as one of my colleagues remarked, I was the first person that he'd known that had been from Kathmandu to Timbuktu to Kota Kinabalu; Kota Kinabalu is on the very northeast corner of Borneo, by the way; very obscure place--led me to have an interest in cultures and perhaps to think about the developing nations in a way different from what many others have thought of them. I think of developing nations now--and I wrote about this in detail in <u>The Next Eighty Years</u>--I think of it as, what we're seeing is a sort of natural selection going on again. Natural selection is testing cultures and individuals to see whether they can succeed in a crowded and an increasingly technologically organized world. Those cultures that can't adjust, like the culture in Bangladesh, are probably just going to die off and disappear. The time will come when it'll be

impossible for us to feed all of the hungry people of the world--in fact, that time's already here, I think. So we're going to see some cultures just disappear. In addition to that, I've learned through my studies, particularly in West Africa and in Indonesia, about the fact that within any given society, in a developing country much more than in a developed country, there's an extremely unequal distribution of wealth. For example, in Indonesia, something like one-half of 1 per cent of the population gets maybe half of the total GNP of the country, including all of the foreign currency, which comes to Indonesia on account of the fact that they sell oil. And these rich people control all the power: they control the generals and the police. They live like normal western-type people; and they have Mercedeses and they practice birth control. And when misery and hunger comes to any part of Indonesia, it's not the rich that suffer; it's the poor peasant whose yearly GNP is about maybe twenty dollars, and consists of what he actually grows on his own very small plot of land. So an underdeveloped country is a country in which there's a few rich people and a lot of poor ones. When I speak about a culture disappearing, what I mean is that the poor people in that land, that culture, are going to disappear; and the rich ones will be left. We're seeing some sort of natural selection beginning to take place; and it's already taking place in Bangladesh for sure. And it took place in the Saharan countries for sure. A lot of the poorest people died off; and maybe the poorest people are the people that are either the least intelligent or the least able to cope. And what we're left with is a population that consists of a subset of the original set of genes of that culture. It's either the genes for being more aggressive or maybe the genes for being smarter. Whatever it is, we're seeing natural selection at work. I'm not so inclined to try to diddle with developing countries as I would have been. I think the do-gooding instinct which the western world's had, and the U.S. has had in particular, has perhaps overall done a lot of bad. We know that when we gave wheat to India, it actually set back the development of wheat-growing in India by quite a number of years. They just grew to depend on our sending wheat there, instead of developing their own agriculture. And I know that when we give weapons to underdeveloped countries, it doesn't do any good: it just makes the strong stronger. And in addition, we give weapons

to foreign countries to make them like us better. And I have been very amused to see such things as in Indonesia, when Sukarno was in power and was leaning very much towards Marxism, but sort of on the fence-ish, and we were giving them airplanes and guns and jeeps and so forth. And Russia always gave them matching grants of their planes and their guns and their jeeps. I've seen it. So I'm very cynical about foreign aid, and I'm doubtful that there's any kind of aid that can be given to a developing country except aid to help to develop education to help the country to help itself. If I ever have time, I'm going to write more books about the developing world and about my thoughts about what we should do about the developing world.

Berry: Do you want to go into any of that here?

Bonner: Well, perhaps; we'll see how it goes.

Berry: I was wondering. In some of these underdeveloped countries where you have a great lot of poor people, don't you think that they'll overthrow the rich as happened in, say, France during its revolution? You say you think that the poor people will die out rather than overthrow the power.

Bonner: Well, this is a good point. And of course, I think that there are cases in which the so-called poor people have overthrown the rich-of which there have been some examples, and perhaps the French Revolution was one; although I think in the French Revolution, the middle class overthrew the royalty. And I'm not quite sure exactly what took place in Iran yet. Somebody overthrew the Shah, but I'm not clear whether it was organized Marxists or whether it was really a people's revolution or both; or whether the repressive measures which the Shah had used to keep himself in power and to which our president, Mr. Carter, objected to so strongly, and he caused the Shah to ease up on his repressive measures. Some people think--and I think it may be right--that it was his easing up on the repressive measures that resulted in his overthrow. But I don't think he was overthrown by poor people. I don't think poor people can overthrow, because they've got no power. Hungry people can't overthrow either; they've got no power. It has to be some sort of organized group that's organized enough to have power and organized enough to get weapons. And that's why I think that in really, truly poor countries like the countries in West Africa. . .yes, in West Africa, to take an extreme example, Uganda--Idi Amin was not overthrown by the poor people, who just feared him; he killed them -- hundreds of thousands of the people of tribes he didn't like. He was overthrown by outside armed forces entering in to dispose of him from Tanzania, and also Ugandan refugees. And he's a sort of a test case because nobody more needed overthrowing than Idi Amin. When I look at Nigeria, which is a very rich country with a good agriculture-at least in the south--and with rich natural resources and lots of oil, and I see that incredible amount of corruption and, again, this extreme maldistribution of wealth and how the power and the ability to use the power all resides in the hands of a very small number of people; and I, on the other hand, go to a village in Nigeria and see the poor peasant farmers growing their sorghum to eat and their peanuts to sell. . . . And their peanuts that they sell, though, could be full of fungal metabolides, which are extremely carcinogenic so that it's really not safe to eat. No kidding. You don't dare eat peanuts in the tropics because they're stored under unsanitary conditions where the peanuts are wet; so they ferment a little bit, and fungi grow in the pile. And the fungi produce a class of compounds called afalatoxins, which are the most carcinogenic compounds that have yet been discovered in the world. A friend of mine in Malaysia, a chemist--who is a nut--started worrying about this problem in Malaysia where they grow lots of peanuts. Lots of peanuts are grown in the tropics, even though storing them presents such a great problem, as I said. He didn't find a single batch of peanuts or peanut butter that wasn't so laden with afalatoxins that he was afraid to eat them. So we don't eat peanuts in the tropical countries. In the U.S. there's a law, you know, that every peanut and peanut butter sample has to be tested for afalatoxins.

Berry: How about Georgia?

Bonner: It's a U.S. law; it's an FDA law. So it's safe in the U.S. That's one of the few places I'd eat peanuts. And this doesn't apply just to peanuts. It's just that peanuts are something that we eat a lot of. Soy beans stored in the same careless way will also get afalatoxins. But of course, we don't eat soy beans on a large scale--although some people do, like Japanese--soy sauce, as do Chinese.

Berry: They're in markets all the time now.

Bonner: Yes, and cotton seeds.

Berry: All this work overseas, that part of the State Department?

Bonner: All the work that Caltech did overseas through this population study group was funded by the State Department.

Berry: And a good many of these places you visited were in that part of the project?

Bonner: Yes. And this program was run by Harrison Brown.

Berry: Not many people know about that.

Bonner: No, they don't know, and I'll come to that in a minute. It was run by Harrison Brown, myself, Allen Sweezy, and Ted Scudder.

Begin Tape 3, Side 2

Bonner: I started in 1970. We held our first international meeting in Pasadena in 1970 in December. And then from then on we held them in Rome because it turned out that if you want to get people from all over the world, Rome is a hell of a lot cheaper place to assemble them than Pasadena. We wanted to have one of these meetings in Singapore because we had several people in Asia. But it turned out it's still cheaper to bring them to Rome than to bring all the people from Europe and Africa to Singapore.

Berry: Now, were there people associated with the program, apparently in different parts of the world that would come to the meetings or what?

Bonner: Yes. You remember the American Universities Field Service? Okay, well, the people that we used as our field officers, field workers, were the AUFS staff. And this was done in collaboration with them under contract with AUFS. And AUFS has some incredibly talented people, some of whom have become our very close friends--like Al Ravenhold and his wife, Marjorie, who live in the Philippines; and Marcus Franda, who was part time with AUFS and part time professor of political science at Colgate, but who has now resigned from Colgate and is a vice president of the AUFS. I suppose he'll become the president pretty soon, succeeding Alan Horton. An absolutely marvelous guy. He was here for "The Next Eighty Years," and gave a very interesting report on Bangladesh and India. He speaks all the languages of the East Indian group of languages. It was tremendously interesting and important. It was decided by the economists--for whom I couldn't have less respect in this matter -- in our division of humanities and social science, that they could spend the money that we spent on AUFS association more profitably in other ways. So we quite AUFS, now for several years. And Ned Munger, who is in fact an AUFS officer graduate, has organized a group of faculty members, including me, who contribute \$100 a year to bring a few AUFS officers to the campus to talk to us and visit. And Marcus Franda will come pretty soon, and Al Ravenhold will be here again. I think it was a gigantic mistake: AUFS was a bridge between Caltech and the outer world--the greater world that most people here never think about.

Berry: Caltech is connected with Washington and a few places. But this work of yours covered the whole. . .

Bonner: World. Absolutely.

Berry: And some of these conclusions that you've mentioned are kind of eye-opening.

Bonner: They may be heretical, but they're correct.

Berry: There are these sob stories that come out. If there were any way to get the food and clothing and everything to the people. . . . But it doesn't always get there.

Bonner: In my report on the Saharan drought and famine, I concluded and I reported that there was absolutely nothing that the U.S. or any other international agency could do, that would accomplish any good. In the first place, you couldn't even think about carrying food to Upper Niger, or Upper Volta. There's no way to get it there, except drop it from airplanes in parachutes. There are landing strips, but they're just dirt landing strips for little planes.

Berry: The creeping of the Sahara itself would. . . ?

Bonner: Yes, it's due to overgrazing. It's been studied a great deal. A report on that was published in <u>Nature</u> a year or so ago. It's everybody's final conclusion. That was my final conclusion, too. But of course, the drought resulted in the dying off of a lot of stock, so it's going to be quite a while before it's overgrazed again.

Berry: Can it recover?

Bonner: Yes. Given enough time. If you go in and thoroughly overgraze a place--and get a lot of erosion--it probably takes somewhere between 50 and 200 years for it to recover.

Berry: Do you have any solution to overproduction?

Bonner: Well, the major problem in the world is overpopulation. It gobbles up the resources faster and faster. You get in the bind that India's in: even though they have, say 2 1/2 percent per year increase in GNP, they have 2 1/2 percent per year increase in population. So everybody stays right where they are. And in some countries, like in Mali, during the period that I was closely associated with it--which is a very poor country to start with--they had a decrease in per capita GNP of about 4 percent a year because of the catastrophic effects of the famine and the increase in the population. People weren't dying as fast as they should have [laughter]. So they had a decrease of per capita GNP that was extremely rapid over a period of about ten years. They got poorer and poorer and poorer. The only hope that I see for the future-and we found this out during the course of our State Department-supported program--(a very important fact) is that in all the countries that we studied except India, people, women, wanted to have less children than they normally get. They welcomed and grabbed onto contraception, and it spread like wildfire in South Korea, in Taiwan, it's also spreading like wildfire in Malaysia. In extremely authoritarian societies like Singapore, Lee Kuan Yew, the prime minister, who's an extremely clever man, has made economic disincentives. There is every opportunity to get contraceptives and take the pill and so forth. You're welcome to have one child; but if you have two, you don't get anymore housing space; if you have three, they give you less.

Berry: It's an amazing place, Singapore.

Bonner: Yes. It's a lot richer per capita than Malaysia now because of its gigantic industrial growth. I was just reading this morning in the <u>Times</u>, again, for something like the third time in a month, a company has ordered three drilling platforms for deep-sea oil wells, built in Singapore. And they're going to be taken around Cape Horn to the Atlantic from Singapore, because this is a good place to build them. They've got the biggest ship-building and ship-repair facilities and experience and dry docks of anywhere except Yokohama.

Berry: In Singapore? Isn't that just a city?

Bonner: It's a city-state. It's like Hong Kong; except it's only half as big as Hong Kong. And it's even better run than Hong Kong because Lee Kuan Yew is a very smart man to start with, and he runs a very tight ship. And of course, the population is very homogeneous. And they really work hard.

Berry: I would think a city couldn't survive by itself. I look at Chicago

and New York going bankrupt. What natural resources do they have?

Bonner: None, except the ingenuity of the people.

Berry: But there's no agricultural back-up in the surrounding areas?

Bonner: No, they have to import everything. Something like threequarters of the population of Singapore live in housing that's been built in the last ten years; and that's in addition to this massive industrialization, the creation of a highly sophisticated electronics industry, and the shipbuilding and ship repair, and the big oil boom in the whole Indonesian region, all the way around to Malaysia, and all the way along the coast of Borneo. That's all being master-minded from Singapore. In addition to everything else, during the last couple of years, companies that have had offices in Hong Kong, international companies, are moving them to Singapore because the cost of living in Hong Kong has gone out of sight. And Singapore's also erected its own banking system, modeled after the Swiss, to get people to keep their money in numbered accounts in Singapore.

Berry: Where do they get all their knowhow? They don't have universities there, do they?

Bonner: Of course they do. The place is full of universities. It starts with the University of Singapore and includes the Singapore Institute of Technology.

Berry: I don't ever remember a Singapore student here, although I'm sure there were some.

Bonner: Oh, we have had quite a few. You just don't recognize them; they speak English, of course.

Berry: Is that the language?

Bonner: Yes, the language of Singapore--English.

http://resolver.caltech.edu/CaltechOH:OH_Bonner_J

Berry: It's an Oriental city?

Bonner: It's all Chinese; about 95 percent Chinese. And there are a few Malays and a few Indians; and a few Caucasians of course. We have friends that live in Singapore--Caucasian friends.

Berry: I know Oliver Wulf liked that city better than any other.

Bonner: Well, Singapore's important, but it's not really so interesting. Hong Kong is the place; no place can compare to Hong Kong. It's so exciting and it's so beautiful. I was in Hong Kong four times this last fall.

Berry: I know twice, when going into China and coming out.

Bonner: Yes. And then I went back to Kuala Lumpur and back, and I stayed in Hong Kong each time. We're becoming old-timers at the Mandarin Hotel. And whenever we get there, the manager comes and greets us.

Berry: I should think so. You've probably been there a dozen times.

Bonner: I've been there 24 times.

Berry: [Laughter] I don't think there's anybody on the faculty here that's more of an international man than you are.

Bonner: Well, there's nobody on the faculty here that's into Asia like I am, so far as I know, except now Clarence Allen. Our faculty has a bad habit of always going to Europe.

Berry: Well, I guess some of the other sciences, yes--physics and biology, too. But biology, as you say, you've taken it beyond the laboratory. In some ways, the world has been your lab. I should think there'd be some awfully interesting books on what you've done. You keep pretty extensive notes? Bonner: Sure. I write memoranda and travel notes on all our travels.

Berry: You haven't written on this subject except in <u>The Next Hundred</u> <u>Years</u> and <u>The Next Ninety Years</u>. Is there a book on the next eighty years?

Bonner: There is. I don't have a copy of that, but you can get it. It's got a red cover that says <u>Eighty</u>, <u>Eighty</u>. You should read that. That's got my views about natural selection within societies, as well as between societies.

Well, it's been awfully interesting. And it's not done yet. And now I want to take up one more thing while we've got time.

I decided five years ago--almost six years now--that the next great step in studying the control of gene expression, since it proved to be impossible to study what genes get turned on and how they get turned on by studying the whole genome, composed of hundreds of thousands of genes, the next great step would be to study genes individually. The possibility of doing this became available six years ago when Dave Hogness of Stanford and Herb Boyer at the University of California at San Francisco and Stanley Cohen at Stanford, each in his own way contributed to the understanding of how to clone foreign genes in bacteria. And so I immediately took that up. And I'm one of the group of cloners here--those that clones genes. I've cloned genes from the rat, because the restrictions surrounding primates used to be very much more strict; they're not strict anymore. I'm trying to study two genes, one of which is turned on in rat liver, and one of which is turned off in rat liver. I'm trying to find out specifically what it is that turns the one on. It'll have to not turn the one that's turned off, on. That's the way I'm trying to study this problem. This is still a very exciting program, but I haven't found out yet. But I'm hoping. And because I have become knowledgeable in the cloning of genes, and because of our many connections in China on account of our many graduate students in China that are living there and are now big shots in China, I was invited by the Chinese Ministry of Education to go in the fall of 1979 to the Genetics Institute of Shanghai and give a month-long course in the technology of cloning genes--so-called recombinant DNA technology. So I accepted, of course, and Ingelore was invited to go,

too, independently of me because she had been acting as a purchasing agent for the Chinese Academy of Sciences. Since we have been separated so long from China, they have absolutely no insight into how you buy things from the United States or anywhere else. They sent a man here once with \$5,000 and a want list of things. And he was unable to spend any of it; he couldn't ever find out how you find a company that makes something that you want. So what they started doing was, whenever a Chinese came here to visit, he'd bring five or ten thousand dollars, and give it to Ingelore and she'd put it in a bank account; and he'd have a want list, and then she'd order the things and send them to China. And now they don't even have to come; they send a check and she puts it in the bank in a special account, and fills their want list. So she gave courses in how to order things and gave them catalogs of scientific companies and tried to help people find out how they could really do this themselves if they'd just put their minds to it. I told her she should open a business, and maybe she will.

So anyway, we went to China, and we were greeted with just incredible enthusiasm and kindness. The Caltech old-boy network just really took hold. Tan Chia Chen, as I told you before, was a graduate student here when I was and also was a student of Dobzhansky's. We had been very close friends--we had made arrangements to go to northwestern China in 1949, and we'd been funded for that travel by the Rockefeller Foundation; but it was aborted on account of the revolution, which we now call "the liberation." So Tan arranged for us to take this same trip in 1979, which we did. We got special permission from the military to go to this region on the Soviet border, and we went to northwest China, which is sort of like Utah and Colorado rolled up in one: high mountains and big deserts, and a salt lake on the bottom of it, and gigantic deserts and mountains. It's just fantastically interesting. We took that trip. We went to see all the things that you go to see--Xian, and the buried, life-sized soldiers and ruins. These soldiers, life-sized soldiers and horses and so forth, were just discovered in 1973 and are being dug out now, actually were buried over 2200 years ago during the Han Dynasty. I taught my class and I gave lectures in all the universities all over China. I got made honorary professor -this letter of appointment [presenting letter] appoints me professor in

the University of Sinkiang, of the Sinkiang Autonomous Region of the People's Republic of China. And I have a badge to show. I've been invited by the president of that university to go again in 1980 and teach their students about cell and molecular biology--it's a very backward university; it really needs help.

Berry: Now, were your lectures in English?

Bonner: Yes.

Berry: Did you have a translator there?

Bonner: Yes. We had a girl that went with us everywhere we went and translated, and she was excellent. She'd been trained for this duty, and we were her first customers. We liked her very much, and we appointed her an honorary daughter. But she was no good at interpreting scientific things. And Tan was no good, because he speaks with a Shanghai dialect, and lots of people couldn't understand him. So there's a man that had been a postdoc at Caltech with Mitchell. He and his wife had both been postdocs at Caltech. A very nice guy named Chin also-there are very few names in China.

Berry: Chin was the fellow who supposedly developed the atom bomb, isn't he?

Bonner: Yes. But he was a different Chin. Our Chin could talk proper Chinese, and he knew all the biology terms. And so he was my interpreter for all my really important lectures. And then I was commanded to go and talk to the vice-premier for science and technology about how to best bring about the modernization of science and technology of China.

Berry: Do they seem behind quite a bit?

Bonner: Oh, they are; they're enormously behind. But they know it. And they're giving a lot of priority to reestablishing education, which was pretty well wrecked by the Red Guards--universities were closed up. Some of my friends suffered incredible indignities. Tan's wife was killed by the Red Guards. She was a Communist party member, and in fact, a rather highly placed official of the Chinese Communist party; but they held a court and decided that she was some sort of back-slider--a revisionist. So they had her executed. Just like that! So now my wife and I have a new enthusiasm: we go to China, and we're going to go there again this year.

Berry: There are several groups in Pasadena going.

Bonner: Yes, but they go in tours. See, we go as a tour of two.

Berry: No, you don't go as a tour, no.

Bonner: No, no. But we're the only people that we saw there that weren't on a tour.

Berry: I can imagine.

Bonner: Even Clarence Allen was on a tour [laughter]. We met him accidentally.

Berry: Did you? Was he on a scientific group?

Bonner: Yes. It was a joint Chinese-American scientific group that was studying earthquake faults.

Berry: Was that about three years ago?

Bonner: No, it was last year. He's been there several times. But he was there last year again. And he went to Tibet to study a great big fault which causes great big earthquakes along the southern edge of Tibet.

Berry: That's where India slammed into Asia, I guess.

Bonner: Yes. Geology is a good racket if you like to travel. Every

http://resolver.caltech.edu/CaltechOH:OH_Bonner_J

place I've been, Clarence Allen is just going or just been there. Like when Ingelore and I went to Soviet Central Asia in 1973 and visited the Seismological Institute which had just been made there, Clarence Allen was coming the next week [laughter].

Berry: Well, there are faults all over the world. You don't need them, apparently.

Bonner: No, you don't have to have them.

Anyway, I want to talk a moment about the genetic lottery. There'd been a lot of talk about genetic engineering and its dangers and so forth. And especially [Robert L.] Sinsheimer was always viewing with alarm, if you remember, about the dangers of manipulation of the human genome-better not play with things like that. So this really annoyed me. And he spoke of the genetic lottery, and I took the liberty of stealing his term. I was invited to give a series of lectures throughout California, sponsored by NASA. So I made a talk, which I thought was a very good talk, called "Beyond Man's Genetic Lottery," which showed all the good things that understanding human genetics and understanding amniocentesis and how to count chromosomes and how to look at cells and find out whether there are bad genes in the fetal cells, how good that would be for us and how, if we don't learn to control our evolution, we'll become extinct, like every other creature always has in the past. This was a good lecture. I gave it as a Watson Lecture, too, subsequently. But Sinsheimer never did react to that. He didn't like it. He's funny: I really don't understand Sinsheimer.

Berry: I remember he had something in $\underline{E \& S}$, where he said that he didn't think that the human mind is capable of some of these new concepts of actually seeing what an atom looked like, or what a gene looked like; that we're too used to thinking in terms of automobiles and houses and whatnot. I hope he changes his mind.

Bonner: Anyway, that's about the genetic lottery. And I never did, in fact, talk about test-tube babies. I did talk about cloning of people. And I remember the first time I talked about that in public was in the Millikan board room. There was a meeting of science writers from newspapers. Do you remember that? Quite a number of years ago. I gave one of the talks at that meeting. I talked about how we could clone people and increase the fraction of population that were geniuses and so forth. Those stories appeared all over the world in newspapers based on my talk.

Berry: A lot of clips from them are still in your file.

Bonner: I got a letter--and this may be there--which was the very best reply I got. It was from a girl in Delhi, India, that said, "I don't know why you had to go and invent a new way of making people; I hope it doesn't work. But if it does work, don't send any of them to India" Elaughter]. And so, in my talk about the genetic lottery, I talked about the new morality--that is, the first morality is that you can only have two children. Next, you'd want to have children that are free of genetic defects, of course. Then, it would occur to people that if you could only have two children, it would be good to have children with the best possible genes; and you'd have to be humble and say, "I won't have children just so I can spread my own genes around; if I have children I owe it to them to endow them with the best possible genes." And that's started a little bit now, with this . . .

Berry: Phyllis Schlafly.

Bonner: Yes. Bonnie Kimball, my former secretary, sent me a clipping from the newspaper this morning. I don't know where she found it. It was a take-off on that, on how all people don't want to have Nobel scientists' genes. Maybe they'd rather have an actor's genes, like maybe Burt Reynolds-type or the Duke or somebody; or maybe a famous football player's genes. And so here's a series of ads for different [types of genes]. One was for an M.D., guaranteed to have an I.Q. of not less than 135 [laughter].

Berry: Was this in public publication?

Bonner: It was in the paper. It was really funny. I don't have it;

Ingelore has it in her office. So, anyway, the new morality idea's really beginning to catch on a little bit. Sinsheimer was really, really funny. He depended on me to do a great deal of work for him, and a great deal of giving talks that he didn't want to give and which I like to give, and a great deal of internal work--like all relations with students I had to handle, because he hated to do that. And at the same time, he was generally quite nasty to me. When he first became chairman, he came to me and he said very seriously, "Now, you appreciate that Caltech has a rule that a husband and a wife can't work in the same division; and so therefore, either you or Ingelore will have to quit the biology division." So I went to Lee DuBridge and I told him what Sinsheimer had said, and he just roared. He said, "That's really nonsense. Furthermore, there must be some sort of grandfather clause about that law that he's invented, so don't worry about it; I'll talk to him." I never heard any more about it Claughter].

And then, early in his tenure, he came to me one day and he said, "James, the first thing you have to do is that you have to give up some laboratory space." And I looked at him straight in the eye and I said, "I won't." And I never heard any more about that either [laughter].

Berry: Would he come to you with student things?

Bonner: Oh, absolutely. Yes. He'd call me on the phone or write notes or send students to me. He never bothered with student affairs at all. You see, I was the acting chairman for two years while Beadle was gone and then while he was trying to decide what to do next. And during that time, I applied for and got this gigantic training grant, which ended up supporting two-thirds of biology graduate students. I got it, and I managed it for fifteen years.

Berry: Was it your grant?

Bonner: Yes. NIH training grant. I was the responsible investigator for that, and was, de facto, really responsible for graduate student affairs. Berry: That would take a lot of work, wouldn't it?

Bonner: Well, yes. Well, it wasn't too bad; I liked it. And then after fifteen years, I turned that over to Horowitz. And just about that time, they started cutting back on the funds for training grants; and I got out just in time, while I was ahead. But it was for that reason that he had to consult me about student affairs, because he really didn't know anything about them.

Berry: Which is a fair part, I would think, of any administrative job.

Bonner: He should have. That's right. He did a very poor job. He was a very part-time administrator, and he did it very badly. And I hope he does better.

Berry: But you never wanted that job?

Bonner: No. I knew enough about it from the time that I was the acting chairman to realize that you spend about a third of your time being a psychoanalyst for discontented professors, and a third of the time talking to people that have got to talk to the chief, and a third of the time talking to philanthropoids--potential donors and so forth--and you don't really have any time to think. I spent some time getting money for rehabilitating Kerckhoff, and got a good start on rehabilitating Kerckhoff, starting with Ray Owen's labs. And not like Sinsheimer: when he became chairman, he started rehabilitating his own labs. One day I was walking around looking at laboratories to see whose needed rehabilitating next, and I found myself enjoying it. I thought, you know, as soon as you begin to enjoy this job, that's the end of one as a scientist. So I quit. DuBridge was really annoyed.

Berry: I can imagine. You took over when Beadle left. I guess you're really glad that you. . .

Bonner: Oh, yes. I think, in the first place, I've had an enormous amount of scientific success since I changed careers in 1960, and more

scientific recognition than ever before. I don't know whether you saw it in <u>Science</u>, but there was a table there of the most cited scientists in the last ten years in the U.S. I was the second most cited--there had been over 9,000 citations to my works in literature since 1970. I had more citations than anybody else that didn't already have his Nobel prize. So I did a lot of work that was interesting and generally recognized. And when I changed from plants to animals, that made a big difference because people in general aren't interested in plants.

Berry: Well, except you did go into some basic biological processes that are common to both plants and animals.

Bonner: Well, that's true, and that worked for a while. But really if it's not true for rats, it's considered not to be true.

Berry: Are you working with those rats now? I remember those peas you were working with--garbage cans full of them. You did a lot of great work with those.

Bonner: Yes. Well, and of course, that turned out to be extremely, intellectually important since it was because we could compare the histones of peas with those of animals that it turned out that this conservation of the structure of histones turned out so quickly and easily.

Berry: So, it's some other thing that tells the histones where to go?

Bonner: Well, no, the histones all go. It's some other thing tells histones to be modified so that they can release their grip on the DNA, so that the DNA can be transcribed. And what this other thing is. . . I got the genes cloned all right--that took several years--and they're very complicated genes, and that's a very interesting story in itself. But now I'm trying to make them into what I'll call mini-chromosomes, with histones and native conformation of the DNA. And now I want to give the enzyme that acetylates histones and makes them let go of the DNA. But I want to give the additional agent whatever it is that must be in the nucleus of liver cells that says only do it to the serum albumen gene that's supposed to be turned on in liver cells, and don't do it to this other gene which is not supposed to be turned on. And this agent either has to be a protein or an RNA molecule. I've got a whole bunch of work that I haven't talked about, going on preparing to finding out all about the RNA molecules that could be candidates, and finding all the proteins that could be candidates.

Berry: Sounds like another several years.

Bonner: I don't have that, you see. I've got to retire in 1981.

Berry: I can't ever imagine you retiring.

Bonner: Oh, I won't retire; but I have to leave Caltech. I've had a whole bunch of interesting things happen. I've been offered two department chairmanships--the University of Arizona, where you don't have to retire, and a deanship at Irvine. But I don't want to do that kind of stuff.