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Adventures in Life and Science, from Light to Rhythms

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Abstract

The author describes her life's pathway from her beginnings at a time when women were not well represented in the sciences. Her grandparents were immigrants to the United States. Although her parents were not able to go to college because of the Great Depression, they supported her education and other adventures. In addition to her interest in science, she describes her interest and involvement in politics. Her education at Oberlin, Stanford, and Harvard prepared her for her independent career at the University of California, Los Angeles, where she was an affirmative action appointment. Her research initially centered on the plant photoreceptor phytochrome, but later in her career she investigated circadian rhythms in plants, discovering and characterizing one of the members of the central oscillator.

Contents

BEGINNINGS

I was born in December 1944, near the very end of the war. My family lived in Louisville, Kentucky. My mother's parents had immigrated there from Odessa, which was then a Russian city, after facing pogroms. Although they spoke Russian to each other, they did not teach it to their five children. My mother's grandfather was a doctor whose immigration was sponsored by a Louisville doctor who was Harvard educated and concerned about injustices in the world. My great-grandfather could not be a normal doctor in the city, although he did some study in Chicago after his arrival. He was sent to practice as a country doctor outside of Louisville, leaving his family during the week. I grew up knowing his children, one of whom, Tyotia Eva, was quite a character: She retained her Russian accent, served as a nurse during the First World War, and wrote poetry that was published in military magazines.

I know much less about my father's family, in part because his mother died from influenza in 1919 when he was just five. His father had immigrated from what is now Lithuania. He worked as an itinerant peddler with a pack on his back, making his way from New York to Louisville, where he stopped and opened a furniture store. I still remember the story of my father as a young boy being so engrossed in what he was reading that his father neglected to notice that he was at the store when it was closed for the night. My father spent a short time in an orphanage before his father found a woman to keep house and care for his son and even younger daughter.

Although my parents were very bright, the Great Depression and their families' poverty made it impossible for them to go to college. However, they always took me on weekly visits to the library, and I loved reading. My mother, concerned about my social development, was afraid I read too much and limited me to one book a day once I was out of elementary school. My grandmother influenced me culturally, taking me to concerts and providing me with piano lessons. I still remember the awe I felt when she took me to a recital by the famous pianist Arthur Rubinstein. She also conveyed her love of opera to me.

Growing up with the fear of a war with atom bombs certainly affected me. When I still was in elementary school, we actually had exercises to prepare for such a war—we went out into the hall and squatted down with our arms over our head and covering our ears and closed our eyes so we wouldn't go blind from the flash. I had nightmares about such an event. By the eighth grade, I was trying to cope with the fear and did a report titled "Atomic Energy." Because my teacher was not exactly an engaged teacher—he was mostly concerned with advising the golf club—he would send us to the library nearly every day to work on our reports. Mine ended up being nearly 100 typed (by my mother, who could type almost 100 words a minute on her manual typewriter) and illustrated pages. In the introduction, about why I chose this topic, I wrote:

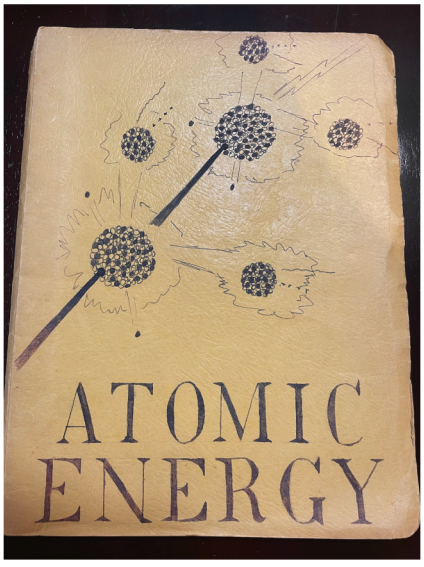

Figure 1

Report on atomic energy from eighth grade.

> I chose the atom and atomic energy because I think it is a very interesting and timely topic. I also believe that in this day and age everyone should know as much as he or she possibly can about this topic. It makes you stop and think a while about what great advances man has made in such a short time, considering how long he has been on the earth, and what a great future he has in store for him if he uses this knowledge carefully.

I still have that report (**Figure 1**).

I enjoyed science classes in high school, particularly chemistry. And my science and math teachers were encouraging. The one exception was my physics teacher, who was also the football coach. He hated that I asked questions he couldn't answer. We reached an unspoken agreement that I would generally skip his class with the excuse that I had to work on the school newspaper or some other school project. My math teacher, Mr. Boyer, recognized that things were a bit too slow in his class and would meet with me in his home to let me progress more quickly. He also was the coach for the boys' intramural basketball team. Basketball was the major sport in Kentucky, and my high school's team were state champions. I participated in a girls' basketball team at the Jewish Community Center and thought I was pretty good at it. When the champion intramural team played a game against the junior varsity team, I convinced Mr. Boyer to send me in! I didn't do much for the few minutes I played, but one of the real team members wrote in my yearbook, "to my basketball idol!" (**Figure 2**).

The zeitgeist of the 1950s in Louisville was very much of the view that a woman would become a wife and mother and help her husband in his career. The closest I came to seeing a female scientist was the lab technician in my doctor's office. I did manage to find a summer volunteer job in a research lab at the University of Louisville, but it was not exactly a first-rate lab. Despite that, I felt committed to research as a career. It is a mystery to me how that occurred, but from junior high on I knew that I wanted to be a scientist and discover new things.

In addition to school, I also became involved in politics and civil rights. When I was 15, my father signed me up to work as a volunteer in the Adlai Stevenson for President office, which was run by a University of Louisville English professor, Harvey Webster. I worked there with

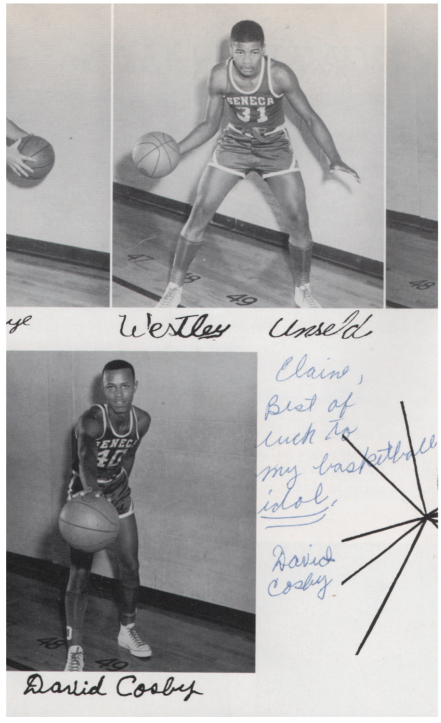

Figure 2

Page from my 1962 high school yearbook, with the inscription, "to my basketball idol." Note that one of my high school team members pictured here (*top right*) was Wes Unseld, who became a famous professional player in Baltimore.

enthusiasm, and as the 1960 Democratic National Convention approached, Professor Webster decided that a few of us should go to Los Angeles to work for the Stevenson campaign. Adlai Stevenson had been the party's nominee in the two previous presidential elections, which were won by Eisenhower. There were only three of us who went to Los Angeles. One was Greta, one of Professor Webster's graduate students, whom my mother entrusted with my care. We went by train in coach class. The first leg was overnight, and when we arrived in Chicago I was shocked when Harvey and Greta ordered alcoholic drinks for breakfast! After we arrived, Greta disappeared and, we discovered later, spent the time with a prominent journalist, then the political reporter for the *Louisville Courier-Journal* and later an eminent editor at *The Washington Post*. So much for my being protected. When I was at Harvard as a graduate student, I saw the journalist again at a reception for the Nieman Fellows. He remembered me from the Los Angeles trip and asked whether I knew how to get in touch with Greta (I did not). In Los Angeles, we were not able to get into the actual convention. We hung around the various campaign offices, and I will always remember the hearty handshake I got from Lyndon Johnson and the brief glimpse I got of Eleanor Roosevelt. I was extremely disappointed when John Kennedy was selected as the presidential candidate. I also managed to convince Harvey to go with me to Disneyland. For me, the biggest thrill in Disneyland was getting to drive a car in Autopia because I had wanted to drive since I was very young indeed. In many ways, this trip to Los Angeles was a bridge for me between being a child and being an adult.

Returning to high school that fall was a letdown, but my teachers, for the most part, recognized that I was a self-directed student and were tolerant of my missing classes to do more important

things, from working on the school newspaper to attending the classes in poetry taught by Professor Webster at the university. He, in fact, became an important mentor to me, providing me with books in modern English literature and poetry. He was involved in the civil rights movement in Louisville, and because of him I participated in marches and was able to see Martin Luther King Jr. when he came to Louisville. He also told me about Oberlin College, where he had studied. The "girls' counselor" at my high school was impressed by my PSAT and SAT scores and told me that I should perhaps consider the University of Kentucky for college. I am afraid that she was not familiar with schools outside of Kentucky. In any case, I graduated as the valedictorian of my class and applied to schools outside of Kentucky. Although I was admitted to Radcliffe (the "girls' college" of Harvard), I felt that Oberlin was the best fit for me after a visit to both places. I was also fortunate in being granted a scholarship by General Motors (GM), a company that gave full scholarships to one girl and one boy in each state each year. The head of the company sent me Christmas cards for some years after I graduated. I suspect that large companies are no longer quite as concerned with the welfare of young people. For me, the excitement of being granted the scholarship was almost outdone by the excitement of the local GM car dealer giving me a car to use for a week!

COLLEGE

Starting classes at Oberlin was a bit of a shock. All of a sudden, students around me were as smart as I was and much better prepared in their high schools. Although I thought I might be a math major, because I loved it in high school, I was shocked by what was expected in the Oberlin course. I had taken a semester of calculus at the University of Louisville the summer before, so I enrolled in the second semester class at Oberlin and discovered that I had never learned to do proofs. I was devastated to get a C in the class, the first time I had gotten anything but As. I had two years of chemistry in high school and an aunt who said that if I was interested in biology, I should study chemistry first. That and Norman Craig, a marvelous chemistry teacher at Oberlin, confirmed my decision to major in chemistry. It was almost undone by organic chemistry my sophomore year. However, in my junior year with physical chemistry, things started to be exciting again. And in advanced organic chemistry, I found that learning the mechanisms of the reactions was much more rewarding than the memorization that put me off in my first organic chemistry course.

After my sophomore year, I was able to spend a summer in Vienna in a program run by Oberlin. I had taken Latin and then two years of German in high school and two more years at Oberlin. I took German originally because my father's sister was married to a chemist, and she advised me that chemistry was the most important science and that the important chemistry papers were published in German. It was in Vienna that I learned to love chamber music. There was a weekly low-priced program of chamber music performed in actual palaces—exactly the places for which the music was composed. I also enjoyed the classes where, in addition to grammar, we read short fiction, and I was introduced to Kafka for the first time. In the free afternoons, I went to the museums, exploring visual art also for the first time. I have to admit that Viennese pastry was another highlight for me. Each week I would scrimp and save the money we were given to find our own dinners in order to afford a visit to Demel. They made the most delicious Sacher torte covered with whipped cream, which I ate in their elegant surroundings.

It wasn't until I was a junior that I took a biology class. It was taught by Tom Scott, one of Winslow Briggs' first students at Stanford. I was thrilled by his lectures on the recently discovered plant photoreceptor phytochrome. As a chemistry major, the idea that a light-induced *cis/trans* isomerization could affect many aspects of plant development was exciting. He also sponsored my chemistry honors research project on auxin. While I worked hard on it, I still don't remember

whether I actually got any significant result. Therefore, I suspect I did not. The best outcome was that after I presented my work as a seminar in the chemistry department, Mr. Craig (although he had a PhD from Harvard, Oberlin professors were still called Mister) said to me, "You would make a good teacher." At the time, I didn't realize what a wonderful compliment that was coming from him and just thought, "But I want to do research, not teach."

I wanted to discover a cure for cancer, which suggests both my ambition and relative ignorance as a 20-year-old. So I planned to apply to medical school. When I asked Mr. Scott for a letter of recommendation, he said that I must not go to medical school if I wanted to do research! I should go to graduate school instead. I trusted him, applied to several places for graduate study, and decided to go to Stanford, where I was accepted by the Biology Department.

WAR ON POVERTY PROGRAM INTERLUDE

Because I wouldn't start until the fall, I spent the summer after my 1966 graduation in a summer program run by Appalachian Volunteers, which was formed in 1964. A representative had come to Oberlin to recruit volunteers for the summer. This was part of Lyndon Johnson's War on Poverty legislation, and I was paid a small stipend from Volunteers in Service to America (VISTA). I worked as a community organizer in Wolfe County, Kentucky, one of the five most impoverished counties in the country. I lived with a family who had three children and who made a living by growing a small plot of tobacco and raising cucumbers for a Louisville pickle factory. The smaller the cucumbers, the more was paid for them. I helped with harvesting them, which was stoop labor, and one had to lift the prickly leaves to find the smallest ones. Ouch. I also learned to "chop backer" (tobacco) and milk their cow. There was only a well for water and an outhouse for relieving oneself, but I didn't mind that. As for the community organizing, I convinced one resident, Darley Dunn, to set up bookshelves for a children's library in his home, and I organized children's gatherings during the day. I also organized potluck suppers to bring together the neighbors along the dirt road, Sandy Ridge, that stretched from Compton, the county seat, to the next county. Some of them suggested that I might help them construct a canning factory, since they all canned their garden produce for winter and felt they were experts at it. I was, however, not capable of helping start a factory. However, in the end, with the help of Mr. Dunn, they managed to form a business selling Christmas wreaths and similar decorations to people in Cincinnati, the closest big city. The book *Reformers to Radicals: The Appalachian Volunteers and the War on Poverty* by Thomas Kiffmeyer (11) describes how the attempted involvement of the group in local politics led fairly quickly to their downfall. They disbanded in 1970.

GRADUATE SCHOOL AND POSTDOCTORAL RESEARCH

That fall I was off to Stanford. I still vividly remember arriving in Palo Alto by train from San Francisco and discovering that after I arrived on campus, it was a walk of a mile to get to the biology building. I felt very small indeed. The new graduate students were housed in the attic of the building, and my most vivid memory is of the student who showed off the newborn mice that he fed to his snakes. He called them jelly beans, which was an accurate description of their shape. I was a bit lost, especially when I discovered that no one in the Biochemistry Department (the most obvious fit for me) would even let me do a rotation in one of their labs because women did not win Nobel Prizes. The department did, however, give a marvelous biochemistry course, which I took and enjoyed greatly. Paul Berg was the teacher in that course who most stands out in my memory. He made even the Krebs cycle exciting by talking about the scientists who investigated it and the experiments they had done.

I also took Winslow Briggs's plant physiology class. It was there that I learned about phytochrome and photoperiodic flowering and the work that Karl Hamner had done on the influence of circadian rhythms on flowering. Thus, the connection between phytochrome and circadian rhythms was brought to my attention early in my graduate career. When I arrived at the University of California, Los Angeles (UCLA) in 1975, Karl Hamner was still there, though about to retire.

In the spring quarter, I was able to rotate into Winslow's lab. He treated me like a scientist and seemed unaware that females were not worth the trouble. How lucky I was to find him! He had just accepted a professorship at Harvard, so I transferred to Harvard for the next academic year.

I was rather surprised that the courses I took at Harvard were so easy compared to Oberlin courses. All you had to do to succeed was listen to the lectures—no further reading of additional material in the library and no challenging exams. I was the teaching assistant for Winslow's plant physiology course and tried to learn something about plants in a prescribed botany course to make up for my total ignorance in that area. I also wrote my first paper on the research I had done in Winslow's lab at Stanford. I labored over it for several months and finally presented it to Winslow. He read it rather quickly and said, "That is a really good abstract, now go write a research paper." Sigh. I did then write one (23), and some years later, Hans Mohr, a German phytochrome scientist, told me that it was so clearly written that he would give it to his students as a good example of how to write a paper.

I wasn't able to do much research that first year at Harvard while Winslow was setting up the new lab. I did meet and marry another graduate student, Allan Tobin, who was in his last year in the program in biophysics. He then wanted to do postdoctoral research for a year at the Weizmann Institute in Israel. Winslow totally supported my decision to spend that year working at the Weizmann and even found a Harvard grant to support me.

Our path to Israel in 1969 involved a charter flight to London, but after that we used trains and then hitchhiking to get across Europe. One of my fondest memories of that trip was of landing in Dubrovnik (which was at that time part of Yugoslavia). There was a summer music festival there, and at the concert that most stands out in my memory we heard Mstislav Rostropovich, who was still in the Soviet Union and not able to travel to Western countries, play in a small concert in the courtyard of a former palace. We then wanted to go to Višegrad to see the Bridge on the Drina. We had read the novel by that name by Ivo Andrić, who had gotten the Nobel Prize in literature in 1961. The novel described centuries of the turbulent history of the area (now Bosnia) centered on the bridge, which was very beautiful. When we asked at the Dubrovnik tourist office how to get there, we were told, "You can't get there from here." Nevertheless, we managed to get there by hitchhiking by way of Sarajevo. It took several days because the area was very poor and there were not many cars. However, the people who picked us up were friendly and helpful. We managed a few words of Serbo-Croatian and they often had rudimentary English. As one can see in the photograph (**Figure 3**), it was indeed a beautiful and substantial bridge, worth all the trouble it took to get there.

Before we started our work at the Weizmann, we spent the summer on a kibbutz in order to learn Hebrew. It was an amazing experience. For half of the day we worked in one of the various enterprises the kibbutz used to generate income. I worked in the chicken coops, where I was responsible for gathering the newly laid eggs that would be incubated elsewhere, and then the day-old chicks would be sold. The hens did not appreciate being lifted off of their nests so I could take their eggs, and I received quite a few pecks of objection (**Figure 4**).

For the other half of the day, we had intensive Hebrew lessons with a marvelous teacher. Israel had developed a highly effective system called an Ulpan to teach immigrants Hebrew. We could speak only Hebrew during each four-hour session, and our teacher insisted that each of us

Figure 3

The Bridge on the Drina, Višegrad, 1969.

respond to questions in the language as we were learning. I ended up with a fluency that was almost as good as my German (not that my speaking of German was very good). I think that my brain has a single compartment for oral language, as evidenced by my experience on a train from Munich to the airport in Frankfurt years later. The train had inexplicably stopped far from its destination, and when I tried to ask my neighbors what was going on, it came out of my mouth in a mixture of German and Hebrew. In any case, for reasons I never learned, I missed my flight.

At the Weizmann, I worked in the laboratory of Ezra Galun in the Department of Plant Genetics. One of the wonderful things about that time was that there were quite a few other American scientists there, and everyone came to the coffee hour at midmorning for free-ranging discussions. I still remember that I got good advice from Chris Anfinsen (who later won the Nobel Prize in

Figure 4

Working in the chicken coops on the kibbutz, 1969.

chemistry) about my research during one such coffee hour. Also remarkable to me at that time was that quite a number of women scientists were there, and some of them were pregnant. Not only that, but after they had their babies most of them reappeared at the lab. Now that is not so remarkable, but at the time (1969–1970) I was not aware of any women who were both mothers and faculty members.

We took advantage of a low-cost airfare offer during spring break to fly to Kenya, where my college roommate, Mary Lavo Ford, was spending the year with her husband, Michael, in Mombasa. Michael had been an early Peace Corps volunteer in Kenya and was pursuing PhD research on Kenyan politics. In 1970, Kenya was independent but still heavily influenced by Britain. When we took the train from Nairobi to Mombasa, we were awakened in our elegant sleeping compartment with tea service delivered. I still remember the thrill of looking out of the window and seeing giraffes while eating breakfast. Before we left Nairobi, we hired a car to visit the game parks. What an experience that was! While we had to bring our own food, it was turned over to the staff at the park and they prepared and served it to us. Our accommodation was in rather luxurious tents. When we went off to explore and look for animals, a local guide joined us in our car. It was a lucky thing for us that he was there to change a flat tire that occurred almost directly under a lion resting on the branch of a tree in the Tsavo National Park. The lions in that park are known to eat people, but he was evidently not hungry at the time. We also took the opportunity to go to Tanzania with our rented car. Here, too, we saw amazing animal life. We also had interesting interactions with members of the Maasai group. Some of them were fascinated by my being white with long, straight black hair, and I once felt as though I was the wildlife being observed as they gathered around me.

When I returned to Harvard, I had something of a struggle to settle on my research topic. In the end, I decided to explore what changes in the protein conformation occurred when the red absorbing form of phytochrome (P_R) was converted to the far-red absorbing form (P_{FR}). I used a number of different techniques and concluded, "The ultra-violet difference spectrum does indicate some kind of a change in the environment of tyrosine and possibly of tryptophan or cysteine" (24, p. 494). Now, of course, the photoconversion is understood in detail (summarized in 16), but my conclusion was true, if limited.

The event that slowed me down a bit was the birth of my son David in December 1971. I was lucky that a child care center had been started adjacent to the Biology lab building, and once he was six months old he could be cared for there during the day. It also meant that I could easily continue breastfeeding him. I discovered fairly quickly that staying at home with a baby was not for me, and so by the time he was six weeks old I returned to the lab along with David. David's father had an appointment as an assistant professor with a lab in the same building, so there was always a backup caretaker. Many of my experimental measurements were made with David on my back in a carrier. Once again, Winslow was supportive, and his attitude was perhaps helped by the fact that he also had a baby of about the same age at home. The only time he made a remark was when we had an older female speaker for our plant biology seminar and he suggested that she might be uncomfortable were I to nurse during her talk. It seemed a rather strange concern to me at the time (and now).

After I finished my PhD research, I accepted a postdoctoral position in 1973 at Brandeis with Attila Klein, who at the time was interested in how light influences the development of land plants. His lab was very small, and he gave me the freedom to design my own research. At this time (bc = before cloning) I took advantage of the latest discovery that messenger RNAs (mRNAs) have a poly(A) tail (2), which enabled its isolation using oligo(dT), and of the development of a technique for translating mRNA in vitro using a wheat germ extract and a radiolabeled amino acid

(15). I had actually met Bryan Roberts, who had developed the technique at the Weizmann Institute, and he showed me his method for making the extract. The radioactive products were then subjected to electrophoresis and visualized on X-ray film. Initially I used tube gels, which made the assays very cumbersome, but one day in the library I came across a paper (3) that described the use of slab gels. I rushed to the workshop with the plans and had them make me such an apparatus, which made the visualization of the results much simpler. I gave birth to Adam, my second son, in 1974. He often accompanied me to Brandeis and was sometimes looked after by Martin Gibbs, the longtime editor of *Plant Physiology*, whose office was adjacent to the Klein lab. My work there demonstrated that plants put into the dark for 24 h and returned to the light for 24 h altered what mRNAs were made (25).

UNIVERSITY OF CALIFORNIA, LOS ANGELES

Thanks to an affirmative action appointment for me and a job offer for my husband, I got my first and only job at UCLA in the Biology Department. When I arrived in the summer of 1975, the department wasn't eager to help me get started and did not provide me with an office, lab space, or much research money. I wrote my first grant application at the desk of a graduate student away doing field research. Fortunately, while I was at Harvard, Lawrence Bogorad had mentioned that the National Institutes of Health (NIH) would fund basic research in plants, so I applied there. In the meantime, we had to organize child care, and we actually started a child care center with several other parents. I was also told that I would have to teach the introductory biology class in the fall quarter. On the whole, my first year at UCLA was quite stressful. I was lucky to be supported by Karl Hamner, who was about to retire and let me use his leftover grant money to hire a technician, something still possible in those days. When my NIH grant was approved, I still needed lab space! So I went to the head of the "space committee" and was told to find some space for myself and that they would approve it. I "found" the Hamner space, which was in the windowless basement of a building that had not been well maintained. It was furnished with lab benches that Professor Hamner had built and painted with gray war surplus paint. Nevertheless, I was happy to have my own space. It also included lots of dark space, which was great for phytochrome research. I improved the bench tops with Con-Tact paper and set off doing research there.

My initial work was carried out with several undergraduate volunteers, a technician, and myself. Once my grant money arrived, I was able to hire two excellent postdocs, one from England (Jane Silverthorne) and one from the Netherlands (Willem Stiekema). With the development of cloning methods, we were able to look more directly at the genes that were phytochrome regulated. We initially worked with *Lemna gibba* (a species of duckweed). I had been introduced to it by Charles (Rusty) Cleland, one of Winslow's former students and at that time an assistant professor at Harvard. It had the experimental advantage of being able to be grown in large amounts vegetatively in a sterile and defined solution, and it was easy to move the flasks it was growing in to different light conditions. We made antibodies to both the small subunit of Rubisco (thanks to Sam Wildman's lab for help with isolating the protein) and a chlorophyll *a/b*-binding protein (thanks to help from Philip Thornber's lab). We were then able to use these to immunoprecipitate translation products from isolated poly(A) RNA to demonstrate indirectly that the mRNAs for both of these proteins increased in response to phytochrome action (22). My first graduate student, Charles Wimpee, collaborated with Jane and Willem to isolate complementary DNA (cDNA) clones for a light-harvesting chlorophyll *a/b* protein and for the small subunit of ribulose 1,5-bisphosphate carboxylase. They then were able to demonstrate that phytochrome controlled the expression of both genes (20).

Still, by just looking at mRNAs, one couldn't know whether an increase was the result of new transcription or decreased degradation. Therefore, Jane set out to look more closely at which was the case by looking directly at transcription in isolated nuclei. During this research, there was an unexpected problem that took a while to track down. It seemed at first that there was no difference in what the nuclei transcribed, whether they were isolated from dark-treated plants or from those given brief red illumination. Was there in fact a light leak in the dark room that might explain that result? Jane and I went into the dark room and patiently waited for our eyes to dark adapt—something that I had learned in Winslow's lab. After about 15 minutes, we realized that we could see each other! Remembering that it only takes one photon to transform one molecule of phytochrome to its active form, we realized that if we plugged the light leak, we might well get a different result. And we did. Jane was able to demonstrate that it was indeed a phytochrome-induced increase in transcription, using nuclei isolated in the dark from dark-grown plants that had been treated (or not) with red and/or far-red light (19). This was the first proof that phytochrome action could affect transcription of specific genes. Soon after, we wrote a review of light-regulated gene expression in plants (26) that later became a "citation classic" (27).

We also collaborated with Philip Thornber's laboratory on an investigation of what is needed for the import of the nuclear-encoded chlorophyll *a/b* proteins into chloroplasts and for their assembly into their final form in the thylakoid membranes (5, 13, 14).

The group of people working on plants at UCLA were generally very supportive of each other and were great colleagues all during my time there. The picture below shows us all before the Plant Physiology building was demolished and after Philip Thornber's death (**Figure 5**).

When *Arabidopsis thaliana* became established as a model plant system, we moved our research to that species. We were quickly able to demonstrate phytochrome regulation of *Lhcb* genes, now more commonly known as *cab* genes, in *Arabidopsis* (9).

We then observed a protein factor that we called the CA-binding factor because it bound a region of a *Lhcb* promoter that was rich in cytosines (C) and adenines (A) and necessary for its phytochrome regulation (10). Next, we isolated a clone for a transcription factor that bound to

Figure 5

Plant biology colleagues at the University of California, Los Angeles, 1998. From left to right: Sabeeha Merchant, Charles West, Sam Wildman, Elaine Tobin, Chentao Lin, Ann Hirsch, Steve Jacobsen, Elma Gonzalez, Bob Goldberg, and Bernard Phinney. Photo provided by Bob Goldberg.

this region. We called it CCA1, named originally for cloned CA-binding factor, and demonstrated that it was necessary for phytochrome regulation of a *Lhcb* gene (28). It wasn't long afterward that my graduate student, Zhi-Yong Wang, expressed the CCA1 clone under a constitutive CaMV 35S promoter in *Arabidopsis* plants. He noticed that when he watered the plants their leaf positions varied, depending on whether he was watering them in the morning or at night. Chance favors the prepared mind, and mine had been prepared by Winslow's class: The circadian rhythms were affected! We went on to show that every rhythm we observed was gone and the endogenous *CCA1* gene was repressed. Thus, CCA1 must almost certainly be a component of the central oscillator in plants. Zhi-Yong went to a meeting with these results on a poster, and someone there had a look at it and said, "That looks very much like what I have seen from George Coupland's lab in England." Panic! However, Coupland had a different but closely related gene (*LHY*) and he was cooperative, so we were able to submit our work together. We also then gave the *CCA1* gene the name *Circadian Clock Associated 1*. The papers were published in the same issue of *Cell*, though I had to argue vociferously over the phone with Ben Lewin, then the editor, that these papers were a real and important breakthrough in identifying two components of the central oscillator in plants (18, 29).

We also studied various aspects of the regulation and function of *CCA1*. One of the interesting observations made by Rachel Green was that plants that had lost circadian rhythms due to the constitutive expression of *CCA1* were less fit than wild-type plants (7). Another important observation was the demonstration that a phosphorylating enzyme, CK2, which can phosphorylate CCA1, is involved in the circadian rhythms of *Arabidopsis* (21). This is one of the few instances of commonality between the regulation of circadian rhythms in plants and the regulation of circadian rhythms in other kingdoms of life.

Both *CCA1* and *LHY* fulfill important criteria for a central oscillator component. They are expressed with a circadian rhythm; their constitutive expression stops all rhythms; they repress their own expression; and, a final criterion, an abrupt transient increase (a pulse) in their expression resets the clock. The last of these criteria had been tested in several of the model systems used to study circadian rhythms. These included KaiC in Cyanobacteria (8), FREQUENCY in *Neurospora* (1) and PERIOD in *Drosophila* (6). Steve Knowles, a graduate student, set out to test this criterion, whether a pulse of *CCA1* or *LHY* resets the clock. In order to give a pulse of each component, he utilized the ethanol-inducible system from *Aspergillus nidulans* (4, 17) to make it possible to induce the proposed component at any time during the circadian cycle by a brief exposure to ethanol. He found that an ethanol-induced pulse of either *CCA1* or *LHY* could indeed reset the phase of circadian rhythms of gene expression (12). Thus, while it had long been widely accepted that *CCA1* and *LHY* are part of the central oscillator in plants, this work definitively proved it.

SABBATICALS

One of the great privileges of academia is the sabbatical. It helps one to learn new ways of looking at one's own research as well as new techniques. By 1982, I was happy to start my first sabbatical along with Philip Thornber, then my significant other and soon to be my husband. We went along with my two sons for the spring quarter to the laboratory of John Ellis at the University of Warwick. David was in fourth grade and adjusted well to school. However, on his first day there, the class was supposed to list the counties of England! He had been a model student and never before had he encountered something in school that he didn't know anything about. He recovered and enjoyed the rest of the time there, particularly playing rounders, a British game equivalent to American baseball. He also learned cricket from Philip, who had gone to Cambridge on something like an

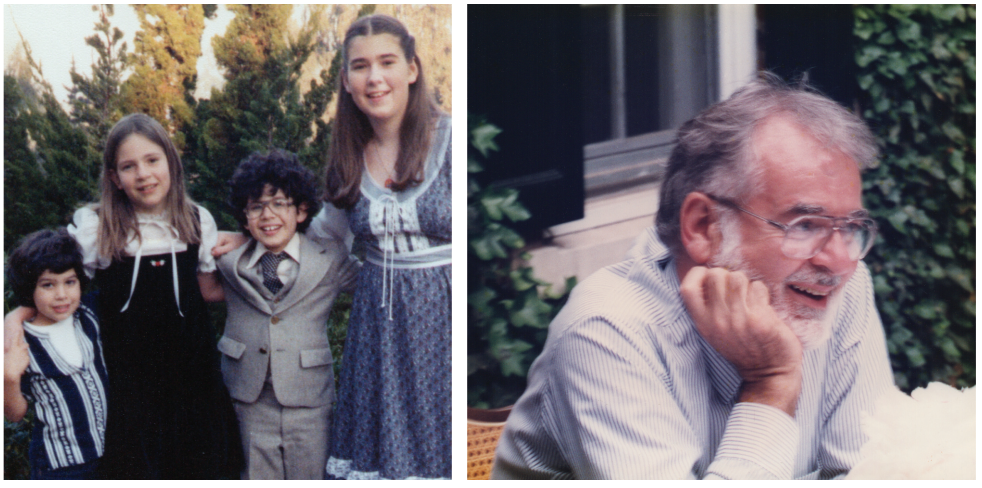

Figure 6

(*left*) Our four children (Adam, Emma, David, and Karen) dressed up for a Thanksgiving dinner around 1980. (*right*) Philip Thornber (1934–1996), beloved husband and father. Photo taken around 1991.

athletic scholarship for his cricket prowess. Adam, age 7, was in the youngest class and seemed to enjoy it, though his teacher was concerned that he was so quiet—the exact opposite of what he was like at home! We then went to Jerusalem for the summer to work in the laboratory of Itzhak Ohad at the Hebrew University. Philip's daughters, Karen and Emma, joined us there. With the four children (**Figure 6**), we investigated much of Jerusalem and quite a bit of Israel. I am afraid we did not accomplish much in the way of science. Eitan Harel, whom I had met when he and his wife Shula spent a sabbatical year at Harvard, served as a wonderful guide to Jerusalem.

Another much later sabbatical was spent in Australia at the Commonwealth Scientific and Industrial Research Organization (CSIRO) in Canberra after Philip had retired from UCLA. I worked in the laboratory of T.J. Higgins, who worked to put genes that could confer pest resistance and improve nutritional value into crop plants. I had the idea that if I could transform *L. gibba* with such genes, it could become an interesting supplementary food source. I worked quite diligently to transform it with a drug resistance gene, starting by culturing it on a defined medium to form callus, bombarding it with the gene DNA, and selecting the transformed tissue on plates containing the drug. Then the plants could be regenerated from the callus cells containing the new gene. I was moderately successful, but I did not get interest from any source that could in fact commercialize it. When I returned to Los Angeles I abandoned that work. The exploration of Australia was a wonderful supplement to the science. There were, of course, the marsupials, various forms of which were all around us. What I hadn't realized before coming was the variety of birds and plants that would fascinate us. At some point, I thought that perhaps I had actually come to a different planet, though there were also many more familiar organisms that had been imported by the British settlers. These imports have actually threatened the existence of many of the native species. During the first part of our time in Canberra, Philip enjoyed learning to cook and having time to pursue art. Those were talents that had been relatively hidden earlier in his life but sprang forth unimpeded now that he had no work responsibilities. Later in our time in Oz, he went to Sydney, where he worked with people at the University of Sydney as an honored senior advisor. I would commute by train to be with him on weekends. We enjoyed the opera and other cultural delights there, and Philip was quite pleased to be able to enjoy cricket as well. It was

shortly after this sabbatical that Philip had some severe health problems that after some months in intensive care resulted in his death.

RETIREMENT AND BEYOND

In the later part of my career, I had some health problems that included an out-of-hospital cardiac arrest. Although I managed to continue to work after a nearly year-long recovery, I found that teaching was stressful and finally realized that retirement might well extend my life. Thus, I chose to retire in 2014. My colleague, Professor Chentao Lin, with the help of Judy Brusslan, a former postdoc, organized a retirement symposium for me at UCLA. It was attended by a great number of my former postdocs and students and also many of my scientific colleagues from other institutions. It was the highlight of my scientific life (**Figure 7**).

Because all of my four children and several of my close friends had moved away from Los Angeles and because my scientific friends were busy with their own careers, I began to feel somewhat isolated. I finally made the decision in 2017 to move to Chapel Hill, North Carolina, where my older son, David, lives with his family. He is now a professor in the medical school at Duke. My younger son, Adam, has a book store in Brooklyn, but, because he decided that New York was not an easy place to raise his young daughter, he now lives in western Massachusetts and commutes once a month or so to Brooklyn to oversee the store. Karen, my older stepdaughter, is a teacher for gifted students in Littleton, Colorado, and Emma has been a librarian at a private school in Connecticut. I am very happy to be in the same time zone as three of my four children and to have the freedom, post-COVID-19, to travel to see them and their children. I am also very happy with living in a cottage in Carol Woods, the retirement community I joined in Chapel Hill. It has given me an easy way to make new friends and to participate in various activities on campus that are returning post-COVID-19. These include concerts; lectures; movies; discussion groups; and my latest interest, semiprofessional-level croquet. I feel that I am living in a self-governing little village with quite a few other retired academics, and, somewhat surprisingly, it reminds me of kibbutz life. One more interesting thing for me has been to see Venus fly traps growing in the wild in an area near the coast—the only place in the world they do so (**Figure 8**).

Figure 7

Photo of me at my retirement symposium, 2014.

Figure 8

Venus fly traps growing in the wild in an area near the coast in North Carolina.

DISCLOSURE STATEMENT

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this article.

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