Birgit Vennesland

Ann. Rev. Plant Physiol. 1981. 32:1–20

RECOLLECTIONS AND SMALL CONFESSIONS

◆7704

Birgit Vennesland

Forschungsstelle Vennesland der Max-Planck-Gesellschaft,
1 Berlin 33, Germany

CONTENTS

The Preacher sought to find out acceptable words - even words of truth

Ecclesiastes 12, 10

On seeking inspiration from the prefatory chapters of my distinguished predecessors, I began to wonder what I had done to deserve inclusion in this series, beyond surviving until retirement. I represent a scientific generation that lived through a developmental explosion when scientific research came of age. Maybe I am typical of those biochemists with plant physiological interests who trained in the 1930s, when refrigerated centrifuges and spectrophotometers and isotopic tracers were only available in homemade versions, fractions were hand-collected, and jobs were rare. My generation has seen greater scientific change in our lifetime than any generation before us. All I can do is describe what it was like.

0066-4294/81/0601-0001$01.00

LIFE HISTORY

I was born together with my sister Kirsten on a stormy November day in 1913 in Kristiansand, a small town on the southern coast of Norway. Ever since, when I return to Norway and look at it, my nose tickles a warning of impending tears. I had forgotten how beautiful it was. This was one of the reasons that I moved, in 1968, from Chicago to Berlin, but that is a later part of the story.

My ancestors, so far as I know, were all Norwegian farmers. My father grew up a country boy, but my maternal grandparents settled in Kristiansand, a town of about 20,000 population. Both my parents attended the normal school in Kristiansand with the object of becoming school teachers, but my father made frequent trips to the USA and Canada, where he functioned variously as a school teacher (in a small Norwegian settlement in Iowa), a bookkeeper, a lumber dealer, a real-estate agent, and finally DDS, graduate of the Chicago School of Dental Surgery.

In May 1917 my parents got tired of waiting for the end of World War I, and my mother bundled my twin sister and me onto a ship to rejoin my father, who had been caught by the war on the other side of the Atlantic. I grew up on the north side of Chicago and attended Waters Grammar School and Roosevelt High School, before entering the University of Chicago in the fall of 1930. Except for two exciting years in the Department of Biochemistry at the Harvard Medical School (in 1939–41), I lived continuously in Chicago until I returned to Europe in 1968.

My parents were liberal-minded middle class citizens, glad to be in the United States—Europe was a rather unhappy part of the world in the 1920s, but life in the USA was comfortable during this decade. We grew up bilingual, speaking Norwegian at home, and our house was always overflowing

tense interest in women's rights, without any urge to participate in politics directly. She maintained an emotional attachment to Norway which was apolitical, but ensured that my sister and I returned to Norway for three extensive visits, in 1921-22, in 1930, and in 1935, so we would not "forget."

I am a product of the public schools of Chicago. In my recollection, they were not so bad. Standards may not have been very high, but we were encouraged to read extensively and to try our hand at writing or debating or acting or singing, or whatever other hobby might interest us. For a period, I was an ardent girl scout, and spent quite happy summers outside the city earning badges for flower,

volved was nonexistent. One acquired handbooks that enabled one to attach a name to what one could see: that was all. But I enjoyed these activities very much and began to think about being some kind of "naturalist." My picture of a naturalist was of a person who spent most of his time collecting things that grew or flew and learning all about them.

The museum of natural history (then the Field Museum) strengthened this interest. For years I spent most of my Saturdays haunting the Field Museum, the Art Institute, and the Public Library in downtown Chicago. I read hungrily and quite indiscriminately. My first favorite fictional characters were probably "Tarzan of the Apes" followed by Jim of "Treasure Island." Robert Louis Stevenson was a little too realistic. I found it cruel of him to give a sore throat to the hero of "Kidnapped."

My father had been prevented by strong pecuniary pressure from entering the occupation he thought he would have liked best, which was civil engineering: bridge building to be exact. In the eyes of the small boy in a wild and mountainous countryside, the man who designed and built bridges was the great hero-figure. My mother had become a school teacher by passionate choice and looked for the same inclinations in her offspring. The result was that when I was asked what I wanted to be, at an age when most boys opted for fireman or locomotive driver and most girls expressed a preference for nursing or acting, I lisped that I wanted to be a teacher. This conviction never left me, but it is hard to say how much was instilled from outside. My mother was a rather compelling educator of the very young. If I search my heart in this matter, I would say that it was the subject matter to be taught that interested me. But what subject matter? Here choice was a little difficult because I was interested in almost everything.

I suppose that under other circumstances I could have ended up in any of a large variety of occupations. But fate took a hand. The University of Chicago offered tuition scholarships to graduating high school students on the basis of competitive examinations. In those years the examination was given in a considerable variety of standard high school subjects, but the examinee picked only one. When invited to take the exam in physics, I was only too glad to say yes. I placed first, with the result that I entered the University of Chicago a little before my seventeenth birthday in the fall of 1930.

From this course of events you might infer that I had a special interest in physics, but that wasn't true. I preferred to take an examination in physics because our high school physics course was taught with a little rigor and was therefore considered "hard." Even in grammar school I had learned that it was much easier to "shine" in a "hard" subject. Later I learned that it had been my great luck that our high school physics course had been a very simplified version of the first year physics sequence taught at the University of Chicago. Had I taken the examination in chemistry, I would have laid an egg. Our high school chemistry course was not taught as a science but as an odd mixture of facts about chemical technology.

In high school I had taken what was then known as a general language major, which was considered, probably rightly, the best college preparatory course. I entered the University of Chicago in the very early days of the reign of R. M. Hutchins, President, then Chancellor, of the University. Hutchins was planning a big reorganization of college education. The class in which I entered was the last class subject to the much-maligned "old" plan. Our successors flourished under the "new" plan, which underwent so many subsequent revisions that one quite lost track of it. But I don't want to get involved in the subject of specialist (old) vs general (new) education. For myself the main point was that I had, so to speak, the benefits of the best of both systems. I was enrolled for the first two quarters in a general science course entitled "The Nature of the World and of Man." This course was staffed by top science professors, each of whom gave a few lectures in his specialty. Most of them were good lecturers. I was spellbound. Since the subject organization was partly alphabetical, we began, I believe, with astronomy and ended with zoology, and I fell in love with each subject in turn, which meant that I began my college career with a decision to become an astronomer and shifted to a committment to zoology, having changed my mind repeatedly over the course of six months. The result of this series of changes was that I chose to follow a premedical program, since it provided for a maximal mix of both physical and biological sciences, at least at the beginning.

I had no real commitment to medicine. Though I dreamed a little of medical research, it was in terms of *Arrowsmith* and *Microbe Hunters* (my major as a premed was bacteriology). I took the first course in biochemistry in the beginning of my junior year, and found myself in a dilemma. From now on it would all be biology. I was finished with the physical sciences, if I continued with my original plan. Though committed to biology, I felt that I needed much more chemistry to think successfully about biological problems. The obvious compromise was biochemistry. There were few BS degrees given at that time with a major in biochemistry, mainly because all of the necessary prerequisites plus a year of biochemistry could not easily be crowded into a four-year program.

The credits on my college transcript showed an appalling concentration on science. As a horrifying example of the uneducated specialist, I was exhibit A. Presumably, I had never read a book except for science texts. This presumption was not true. I had actually done all the assigned reading for the "survey" courses in the humanities and social sciences plus most of the assignments that Hutchins and Adler gave in their "Great Books" course. It was my exceeding good fortune that I went through college with my physical wants provided for in the University dormitories and no need to earn my way by taking part-time jobs. Thus, I had plenty of free time to indulge in hobbies, and I have always been a voracious reader with rather catholic tastes. It only enhanced my pleasure that I could read St. Augustine and Dostoevsky and Democritus and Hume for fun, without subsequently being subjected to the indignity of a multiple choice examination. The use of such examinations as a measure of the well-rounded human being is in my opinion a barbarism. The important thing in the humanities is the exposure to the works of great thinkers and artists. For this the University of Chicago in the early thirties was an excellent place. One could attend or cut any lectures one pleased, and the libraries were open til ten in the evening.

Becoming a Biochemist

I took my BS in biochemistry in the spring of 1934 and spent five subsequent months working as a chemical technician in the department of medicine of the University of Illinois Medical School on Chicago's West Side. That was my first taste of earning my own living. The work was not uninteresting, because I was attached to a research project, but I realized that I had still only scratched the surface of what I needed and wanted to know if I was going to do research in biology. In the fall I returned to the University graduate school in the same department of biochemistry.

The decade of the thirties was not a happy time in the graduate schools. It was the decade of the great depression. Most students had to live on a shoestring. The department of biochemistry happened to be better off than most. It provided its graduate students with teaching assistantships: $ 200 for each 12-week quarter = $ 800 per year, from which a minimum of 4 X $ 33 = 132 was repaid as tuition. A single person could almost live on the remainder, though not with any frills. We took outside jobs wherever we found them. I remember doing pH determinations for the meat packers, with a homemade glass electrode. The necessary special glass had just become available commercially.

In *The Adventures of Augie March,* Saul Bellow has described the milieu around the Midway in the thirties. His time there coincided apparently in part with mine and our paths probably crossed. Though I have no clear recollection of having met him, I have suspicions. But the picturesque squalor described by Bellow wasn't so picturesque (or squalid either) for the graduate science students. We spent most of our time, morning, noon, and night, in the laboratory. Meals were cooked there, and romance sometimes flourished there.

Throughout my years as a student of biochemistry at the University of Chicago, Fred C. Koch was Departmental Chairman. Koch's research interests were in steroids, both in the form of vitamins and of sex hormones —a very ambitious program. In addition, he was interested in the development of analytical methods suitable for use in the clinical laboratories attached to the University hospital. In the student training there was a heavy emphasis on blood and urine analysis. This had good practical reasons. Hospital laboratories provided jobs for biochemists, and jobs were a very precious commodity.

The biochemistry of the thirties was mainly concerned with the chemistry of small molecules. Vitamins, hormones, and growth factors were being identified. From the chemistry of carbohydrates, fats, and amino acids, we made a conceptual leap to the physiological aspects of diabetis, ketogenesis, and glyconeogenesis. In between there was the very mysterious process of metabolism which took place in something equally mysterious called protoplasm and was catalyzed by agents called enzymes.

Enzymes, we were taught, were of unknown chemical nature. This may seem surprising, since Sumner had long since identified urease as a crystalline protein, and Northrop and Kunitz were crystallizing the proteolytic enzymes of the digestive tract. But Fred Koch was a great admirer of Willstätter, and adhered to Willstätter's view that peroxidase was not a protein. It has been pointed out that Willstätter, who was a first-rate chemist, had the sheer bad luck of selecting for purification an enzyme with a very high turnover number. He purified it to a point where the available protein tests were negative and the material left no ash, though it still gave a good enzyme test. (This business about the ash was the origin of a certain friction between Willstätter and Otto Warburg, as described in a later section.)

The opposition to the conclusion that enzymes were proteins was not irrational. The prevailing view was that "proteins are big polypeptides. Such molecules do not have catalytic properties. They can absorb other substances, however. The isolation of a few crystalline proteins with enzymatic properties is the result of the absorption of the enzyme on the protein." What was actually demanded was the isolation of the active center of the enzyme. Later the identification of special prosthetic groups for various reaction types made the notion that enzymes are proteins easier to accept. But what really clinched the point was not one single discovery but a massive accumulation of findings with many different enzyme reactions, showing that no enzymatic activity could be separated from protein.

For my PhD I picked my own problem with Martin Hanke's sponsorship and help. By 1938 I had completed my thesis on the *Oxidation-reduction requirements of an obligate anaerobe.* This thesis didn't, in my later opinion, amount to much. I was trying to approach the problem of what it was that distinguished obligate anaerobes from other bacteria, and I didn't select a very good approach. But the work taught me two things: It taught me that bacteria require CO_2 for growth, and it taught me the importance of collaborators. If you have to do absolutely everything all by yourself, progress can be very slow, especially if you have no money.

Boston and Radioactive Carbon

After working for a year as research assistant for E. A. Evans, Jr., I had the colossal good luck in 1939 to get a fellowship from the International Federation of University Women. This fellowship carried the stipulation that it had to be used in a foreign country. Arrangements were made for me to join Meyerhof, who was at that time in Paris. A summary and evaluation of Meyerhof's scientific achievements can be found in Nachmansohn's autobiographical chapter (5), in which the latter also outlines the problems faced by Meyerhof in 1939.

I was to leave for Paris in the middle of September. On the outbreak of World War II, all passports of American citizens were cancelled. You had to reapply for a new one in order to go to Europe, and you had better have a good reason. This was at first a bitter blow. In retrospect, however, it is clear that the fates had been kind, because I managed to find sanctuary in Baird Hastings's department of biochemistry at the Harvard Medical School. When I arrived, he assigned me to his ^{11}C-glycogen project, which was just getting organized. As a departmental chairman and group leader of the ^{11}C project, Baird Hastings was one of the kindest and most considerate human beings that I have ever encountered. He ran a happy department in an unhappy time. The following two years were for me depressing in terms of the continual escalations of the war; and at the same time they were intensely stimulating and exciting as far as scientific work was concerned.

The utility of deuterium for studying metabolic processes or paths had recently been demonstrated at Columbia by Schoenheimer and his coworkers, but the usefulness of D was limited. ^{11}C was the first radioactive isotope of carbon made available to biochemists. It had a half-life of about 20 minutes—a severe limitation which required speed in all operations. There was a substantial group involved. To achieve the necessary velocity, four or five people actively participated in each labeling experiment. We studied the synthesis of glycogen by rat liver in vivo, with the object of learning something about how glycogen was made from precursors of low molecular weight. The most interesting discovery was that the carbon of CO_2 got into the carbon of the glycogen. There were several laboratories working on related reactions at this time, more or less unaware of each other. The full story has been told elsewhere (2) and calls for no recapitulation. Earl Evans, who had been working with Hans Krebs in Sheffield, came back to the University of Chicago in 1940, got hold of some ^{11}C from Louis Slotin, and showed that the α-ketoglutarate, made during the Krebs cycle by pigeon liver brei, was labeled by $^{11}CO_2$. In the fall of 1941, I returned to the University of Chicago as an Instructor of Biochemistry with the intention of continuing ^{11}C experiments with Evans and Slotin, but we didn't get much accomplished before the United States was also involved in the war. During the following year or so, the chemists who could make and handle isotopes were swallowed by war projects, and research unrelated to the war effort ceased almost completely. I was attached to a Malaria project, but my teaching assignments were so heavy that there was time for little else.

In retrospect, when I revive my recollections of my two years at Harvard, it seems to me that there was an electrical intellectual excitement in the Boston air. This was partly due to ^{11}C, but there was also something else. It was the time of the great migration of scientists from Europe to America. They came first to the eastern seaboard and often gathered in Woods Hole, which was within easy weekend reach of Boston. Through Gertrude Perlmann, I had an opportunity to read Fritz Lipmann's paper, "Metabolic Generation and Utilization of Phosphate Bond Energy," when it was still in press in Volume 1 of *Advances in Enzymology*. This manuscript seemed to have the power of a revelation. Now I could understand why Meyerhof had suggested that I work on the "oxidizing enzyme" of glycolysis. Now I felt that I understood glycolysis for the first time. Of course it wasn't until the postwar years that the biochemical seeds sown by the immigrants grew and bore fruit a hundredfold.

β-Carboxylations and Stereospecificity

When things began returning to normal after the war was over, I turned my attention to plants, with the object of looking for dark fixation of CO_2, Krebs cycle, and other enzyme reactions. The known facts about the metabolism of *Crassulacean* plants suggested strongly that a set of reactions similar to those of the Krebs cycle plus the dark carboxylations known as Wood-Werkman reactions, would probably be found in plants also. I believe that what attracted me to higher plants as experimental material was the paucity of information available about their metabolism, plus the fact that they were the seat of one of the most fascinating processes in nature: photosynthesis.

James Franck and Hans Gaffron were located in a neighboring building, and I often went over to listen to their seminars and discussion groups, in this way learning also a good deal about the history of the photosynthesis problem and the development of current experimentation. Since different research groups at the same institution were not supposed to compete, it was agreed that I would limit myself to dark reactions, unless it was possible to find an area for collaboration. My group had invested much time and effort in the preparation of the pyridine nucleotides, and Eric Conn gave some of our TPN (NADP) to one of Franck's students (Tolmach), who was overjoyed when it worked as a reagent for eliciting O_2 evolution. But no real collaboration developed here, mainly because James Franck didn't like enzymes. I suspect that the root of this antipathy was similar to the root of Otto Warburg's unreasonable antipathy for radioactive isotopes. After a certain age, it becomes difficult if not impossible to master a new technique. It happens to all of us.

It was about 1949–50, as I recall, that Frank Westheimer of the Chemistry Department and I discovered that we were both interested in β-carboxylations, except that he, of course, was interested in reaction mechanism, whereas I was looking for enzymes that catalyzed such reactions. When Harvey Fisher asked if he could do a joint PhD with Westheimer and me, I rather expected that what would emerge would be a carboxylation project. But no, what Westheimer wanted to work with was pyridine nucleotides. He had been using deuterium to study the mechanism of oxidation of alcohols by chromates. (That problem, Harvey informed me, was known as "how to make better cleaning solution.") Now Westheimer wanted to know how diphosphopyridine nucleotide (NAD) and alcohol dehydrogenase oxidized ethanol. Hydrogen must either be transferred directly, or the extra hydrogen in the reduced pyridine nucleotide must have its origin in water. The problem was beautifully formulated from the very beginning. By great good luck, Pabst put diphosphopyridine nucleotide on the market at just the right time, so that the preparative work required was simplified. The first serious experiment was successful. We soon knew that there was direct transfer of one hydrogen atom. Since Ogston's celebrated paper (1) had appeared, and we had sweated out the significance of Ogston's paper in connection with citrate synthesis, as told elsewhere (7), the possibility of using deuterium to do stereospecificity studies was apparent. All in all, this was a happy and very successful collaboration, perhaps because Westheimer and I brought different past experience and skills to a problem of common interest. What little I could contribute to mechanism studies rests on the tutoring I received from Westheimer.

A summary of known information about the stereospecificity of hydrogen transfer in pyridine nucleotide dehydrogenase reactions has appeared (8), and there the reviewers give me a little more credit than is my due for getting this work started. That isn't quite fair to Westheimer, though I feel a flush of gratitude to the reviewers. But when I think of the long line of students and postdocs who worked on this project and contributed all the hard labor, I feel very humble indeed. I do deserve credit for durability. Perhaps I stuck with it longest.

Photosynthesis and Otto Warburg

After Gaffron left Chicago, I began to work seriously with chloroplast preparations, trying to learn something about photophosphorylation and the Hill reaction. A fact that particularly caught my fancy was the catalytic effect of CO_2 on the latter. Warburg was putting a strong emphasis on this point because it fit his theory of photosynthesis. Gaffron said Warburg's experiments were irreproducible. I decided to try it myself, and found that one could get quite good stimulation of Hill reactions with CO_2, provided one picked the right conditions. This was the background for my initial visit to Warburg's laboratory in 1961.

A succession of visits ensued and culminated in my accepting a position as a director at Warburg's institute in West Berlin in 1968. There I began to work on nitrate reduction by *Chlorella*. There were complex reasons for the selection of this problem. One was that Warburg regarded nitrate as the "natural" Hill reagent. Later I gradually developed a strong suspicion that the reason Warburg got such fantastically low values for the overall quantum requirement of photosynthesis was mainly that he had nitrate in the medium and excess carbohydrate in the cells. Better methods have long since superseded those used by Warburg, and the problem of the quantum requirement is no longer cogent.

The editors made it clear that I was not to write a scientific review, so I will exercise heroic self-restraint and refrain from saying much more about nitrate reduction.

Warburg's theory of photosynthesis was sensible and internally self-consistent, though it paid no attention to any experiments that he hadn't done himself. There were some assumptions in his theory and he was quite aware of them. I asked him once whether he didn't think there might be more than one kind of light reaction. "Of course, there might be. But you should keep everything as simple as you possibly can. Never introduce any more detail into a theory than you must." Me: "But, Herr Professor, I think there is evidence that there are two different kinds of light reactions." Warburg: "What is your evidence? Have you seen it?" Me: "Well, not exactly—uh. There is lots of evidence from different labs." Warburg: "Don't tell me about anybody else's experiments. I want to see yours. Show me. That's the way one should argue. I'll show you my experiments. Then you show me your experiments." Me: "All right."

When I last looked at Warburg's desk, it looked as though he was doing energy calculations for an equation which I had suggested to him:

$$H_2 + HNO_2 \xrightarrow{h\nu} NH_3 + O_2 \qquad 1.$$

I had thought of this formulation when I was reading his earlier work on nitrate reduction. The advantage of Equation 1 over Warburg's earlier formulation was that the new equation is really a one-quantum reaction, almost. Now one didn't need a back reaction of O_2 to make up the energy deficit, and CO_2 was pushed over to the Calvin cycle where it belonged. Had it been possible to convince him that there was a second light reaction that caused dismutation but led to no O_2 evolution, he might have added:

$$NH_3 + HOH \xrightarrow{h\nu} NH_2OH + H_2 \qquad 2.$$

and

$$NH_2OH + HOH \xrightarrow{h\nu} HNO_2 + 2H_2 \qquad 3.$$

All three equations add up to look like water-splitting, but in principle they represent an attempt to divide the overall process into three chemical steps, each of which might be energized by one light quantum.

In my opinion, the apparent naivete in Warburg's theories was studied and intentional. The rules seemed to be: keep maximal simplicity and stick to minimal numbers. Make changes only when you must. The advantage of writing balanced equations is mainly that it is an indispensable approach to correct energy calculations. The chemical identity of the components need not be taken literally. One knows that the entire process is far more complicated than the symbols suggest. The very starkness of the symbols protects one from the easy semantic error of confusing the picture with the phenomena that the picture represents. To me, this approach to theory building seems preferable to the currently accepted practice of beginning with a diagram of an hypothetical electron-transport chain. This latter term, invented to represent a sequence of reactions in time, has been converted in the minds of many to a real chain along which electrons flow. Arguing about the properties of such chains is a little like counting angels on the head of a pin, though it seems to pay.

Lest the previous paragraphs give the impression that my relations with Warburg were totally harmonious, I hasten to add that the harmony was mainly confined to scientific questions at a fairly elementary level. Warburg was a man of violent emotions. Anger was predominant, and he wasn't very rational when his emotions took control. We all have a rational self and an irrational, emotional self. Mostly, the rational self is in control. Warburg's emotional self was unusually powerful. Science was his recipe for staying rational.

A mutual acquaintance—not a scientist—was reported to be so disappointed in an emotional relationship that he got sick. Warburg's advice was, "Tell him not to think about anything but science—think about absolutely nothing else—only science." Since the sick man was not a scientist, this prescription probably didn't help him much. But I regard it as a clue to the reason that science, for Warburg, was such an obsession.

On a visit to Warburg's laboratory, I had asked him once for his opinion about the claim in an earlier biographical sketch that Warburg had never made any mistakes. He pondered awhile and said, "Of course, I have made mistakes—many of them. The only way to avoid making any mistakes is never to do anything at all. My biggest mistake—", here he paused a long time before continuing, "my biggest mistake was to get much too much involved in controversy. Never get involved in controversy. It's a waste of time. It isn't that controversy in itself is wrong. No, it can even be stimulating. But controversy takes too much time and energy. That's what's wrong about it. I have wasted my time and my energy in controversy, when I should have been going on doing new experiments, and now—". In the course of the conversation, Warburg also tried to explain to me why he got so mad at James Franck. Warburg: "He said—he said—I couldn't measure light. He was a theoretician. By himself he couldn't measure anything, and he said I—I couldn't—measure—." Something curious was happening. Warburg was getting a little incoherent. In the course of telling me about why he got angry, Otto Warburg got angry all over again. He got as angry as he would have been if James Franck had been sitting there in the same room, now, telling him how sorry he (Franck) was, that his (Warburg's) measurements couldn't possibly be right. At that time, however, I hadn't learned to recognize Warburg's anger. He didn't usually signal it the way most of us do, by raising the pitch and/or the volume of his voice. He had perfect control over his behavior.

Warburg's views on photosynthesis could be considered to be a further development of Willstätter's views. The well-selected library of the Institute for Cell Physiology included Willstätter's works on chlorophyll and photosynthesis. But there was an antagonism to Willstätter on Warburg's part. What was its origin? Warburg told me about this as follows:

> Willstätter gave a lecture about peroxidase and the audience was very big. When he had finished and it was time for questions, I asked him if there was any ash. That wasn't such a stupid question for a young man to ask, was it? Willstätter said, "No, Herr Warburg, there isn't any ash." It wasn't what he said, but the way he said it. He was a good speaker. Because of the way he said it, five hundred people laughed.

In his fine biography of Warburg (3), Hans Krebs cites two sentences concerning the 46-year war over bioenergetics as an example of Warburg's often very aggressive polemical style. I translated the original German version of that manuscript into English. Warburg asked me to do this for him. Now I know perfectly well that the translator isn't supposed to try to improve on the original. He is supposed to be accurate. I did the translation as conscientiously as though I were taking an examination for a translator's certificate, except at one place. After pondering carefully, I translated the "war" into "argument," knowing that this would flunk me. Except that I thought the examiner wouldn't notice. The examiner, I assumed, would be Warburg himself. At first, this guess seemed right. Warburg concentrated on the science and didn't notice the omitted war. He was pleased and complimented me on how well I understood his experiments and theories. Since he was never prodigal with compliments, I felt pretty good. But there was a second examiner, a Warburg No. 2, who acted as a censor. I hadn't known about him. The censor didn't know any science, but he could read English. So the day after getting the nice A, I was told my grade had been changed to an F. "I won't use any of it," said Warburg, in anger. The baleful glare of his blue-gray eyes could be uncannily frightening. Of course it didn't help to try to point out that I was only giving his own advice back to him. Advice is a commodity that can readily be transmitted from senior to junior, but seldom in the other direction.

Warburg was a stubborn man, and apparently something of a rebel in his youth. In German universities there is a procedure called habilitation, which qualifies a person to hold a professorship. This procedure is a kind of final examination, in which the candidate demonstrates his teaching competence as well as his mastery of a research area. Warburg was proud of the fact that he had never submitted to the habilitation process.

Krebs has told how Warburg became a professor by sending lamb chops to Fisher (3). Warburg told me once how he first managed not to become a professor. Warburg: "I have never given a lecture to students. Never. Not one. When I was young, my Professor said, 'The time has come. You have to give some lectures.'

I said, 'I won't.'

He said, 'You must.'

I said, 'I won't.'

He said, 'Oh come, just a few, not many, you can easily do it.'

I said, 'I won't.'

So they held a meeting and decided it must be schizoid-paranoia." Warburg smiled when he got to the last sentence.

In a book review, I once wrote a kind of sketch of Warburg (6). His comment, on reading this review was, "How nice, how very nice. But I am not like that. Really not. You are mistaken." Indeed I was mistaken, as I later discovered. Up to that time, I had seen only the sunny side of a very complex character. The brightest sun casts the darkest shadow.

I hope Warburg approves of the present manuscript, as he once did of another one. This latter paper described some work that had been done in his laboratory, and was dutifully mailed to him for his approval. That manuscript crossed the Atlantic six times. After two revisions I finally got the hoped-for letter: Dear Dr. Vennesland: Imprimatur! Warburg.

SOME PREJUDICES AND OPINIONS

The editors have given me laissez-faire. I can express my prejudices and opinions without editorial censorship. After a lifetime subjected to the discipline of science editors, I find this new freedom heady stuff. Here we go! Let me apologize for the next section by explaining that it is not completely factual; but it contains some grains of truth, nevertheless.

The Problems of Scientific Publishing

These are so great that I am going to have to switch to parables. The journals, some of them, are making brevity such a virtue that clarity has become a sin. It isn't that I have anything against editors. Editors work hard for little or nothing but the glory of having their names appear in public; and the job is usually sheer drudgery. Editors deserve our gratitude for the time and effort they invest in preserving high standards. OK. But there's more to the job of an editor than that. I demand that the editor use his head before I'm going to give him any gratitude.

Here is parable 1. I once got a rejection slip from a well-known journal saying that there might have been some interest in this material if the work had been done with a purified enzyme, but since all of the work had been done with nothing but crude extracts, it was totally unsuitable - oh - you know the usual lines. They were accompanied by a more soothing suggestion that I try another journal. Now, Ladies and Gentlemen, imagine my feelings! I know you can. Half of that paper dealt with experiments with purified enzyme! Imagine my feelings - pardon - my becoming a little incoherent. That bastard hasn't even taken the trouble to read my paper. Imagine? *My* paper! That's what my feelings were. Now it turned out all to the good, because the paper probably *was* more suitable for the second journal, and it was also revised for the second journal and became a better paper. This time we put the last half in front and the front half in the back. I couldn't resist that final slap at the anonymous referee who wasn't interested in my paper.

My second parable is inspired by a horrifying suggestion that I recently read somewhere—perhaps in TIBS—that referees should be named and authors should be anonymous. When I act as referee, I try to make my hands soft as silk. I am not an intemperate critic when I am writing anonymously to a defenseless author. I know who he is, but he doesn't know me. He can't hit me back because he doesn't know whom to hit; and I have never enjoyed slapping defenseless children. But an editor once had the nerve to write to me, to ask me for my opinion of a paper by an unidentified author. This isn't the normal kind of request made to a referee. The referee is usually told who the author is. Now, I'm not to be told who the author is, but of course the editor knows who he is, and the editor wants my honest opinion, so the wise editor can protect the author from injustice, can't he? So what did I do? I blasted that author—oops that was a Freudian slip—I mean editor—no—I mean author—who do I mean anyway?—with the roar of all the cannon I have in my artillery! "I don't know who the author is, but in my opinion the paper shows that he doesn't know what he is talking about. The following two examples should suffice, etc. I hope that these are written in a form suitable for transmission to the author." I never received the reply of the outraged author. It was probably unprintable.

Women in the Universities

I have already mentioned the debt I owe to the International Federation of University Women. It seems obligatory to comment on the women's rights movement with its attendant publicity, which has been louder in the USA perhaps than in Europe. First of all, I feel a genuine sisterly sympathy for any young woman who is determined to make her way in a research career, and I am glad that it has been recognized in principle, at least, that women should be considered for assistant professorships and promotion on the academic ladder on the same basis as men. Reverse discrimination, however, bothers me very much indeed. I do not approve of it in any form. In the long run, such a practice will guarantee a lower average quality in academia. In other words, I don't think that one should try to establish a particular sex ratio for academic appointments in too short a time. And I don't even think we should try to calculate what an appropriate "fair" ratio of sexes should be. Maybe the men really do have brains better suited to perform best in hardware subjects like physics. Maybe the girls have brains better suited to perform best in biology? Let's let the optimal mix demonstrate itself.

The entry of women into public life in more than occasional numbers is a fairly recent phenomenon in human history. The cause undoubtedly lies in underlying economic changes, the same ones that have caused a large population shift from country to city. If we go back several hundred years to colonial America or to Europe in the eighteenth century, most of our female ancestors were living on farms and engaged in a form of housekeeping that was a full-time job. The raw materials often came straight from the field. It was the man's job to provide them and the woman's job to convert them into daily meals and clothing. The upper classes had servants, true, but these rulers were a tiny minority. The great bulk of the population lived like Adam and Eve, delving and spinning, and no one questioned the importance of the woman's job for the family prosperity. What has housekeeping become now? Every single task has been lightened with labor-saving devices to such a point that fewer and fewer able-bodied women can take pride in their housekeeping performance as a difficult job well done. With the exception of the care of small children, which I grant is an all-consuming task, women are left with no satisfying occupation except for the period of child-rearing. The consequence is that women move into the market place in increasing numbers, demanding a share of the more interesting positions and society is adapting to this change. My impression is that most men view this movement with sympathy and understanding. Their wives and daughters are involved. And take note, you blacks and women, who demand instant action. Take note: If you get all the reverse discrimination you want, this will provide what some will regard as proof that you really are "inferior." And you ought to be able to figure out what that proof will be. Most of the intellectual lightweights on the staff *will be* blacks and women.

Research Financing

The support provided for the individual scientist by the Max-Planck-Society is ideal. I have nothing but gratitude for this support and for the manner in which it is administered. Since my move to Germany preceded the crunch in research funding in the USA, my experience of research poverty is limited to the thirties, which is a long way back. Nevertheless, one's earlier recollections are often the most vivid. My generation could have accomplished much more if we hadn't been forced to spend so much of our time on do-it-yourself activities. Though this was not totally bad training, it seems reasonably clear that one individual cannot aspire to becoming an expert glass blower and instrument maker, bench chemist and lecturer, as well as an authority on the theoretical aspects of his subject. Even if the talents for these occupations are all there, human life is too short to acquire the necessary expertise in all crafts and disciplines. The provision of positions with other positions attached to make a unit recognizes this need for cooperative productivity. The problem of hierarchy (who is the boss?) remains, and is solved in the Max-Planck-Society by providing real tenure only for the top positions. Isn't there room here for an adjustment?

In some areas, seven independent groups of three or four scientists may be more productive than one group of 25. This is a plea for more intermediary tenure positions at an independent level within the Max-Planck-Society. I grant that there are problems which can only be handled by very large units, but only a fraction of biological research is of such a nature.

Science: A Personal View

I have never before attempted to articulate my view of the natural sciences. When I was still quite young, formal philosophy appealed to me, but its attractions gradually vanished as I immersed myself in the study of living things. The contents of this section reflect this transition, and are personal in the sense that they express tastes or preferences which are bound to vary with the individual. But I have attempted also to express as clearly as possible my own rational view of the relationship of a self-conscious human being to the universe of changing things.

Scientific thinking is thought about the real world. A mind trained (or untrained) in classical logic has a tendency to confuse scientific thinking with the thinking of classical logic because the logic is the same. But scientific thinking does not permit the use of symbols, concepts—call them what you will—unless they stand for things that are real. Therefore, it is very important to be especially careful to examine the real meaning of the words we are using.

Logic is an internally consistent system of thinking. Classical logic is expressed in terms of symbols and speech. These entities need have no correspondence to the things of reality. Classical logic is attractive to the young mind which knows speech but doesn't know much more. The young mind likes to dance. Logic is the dance of the mind. Classical logic is the art of reasoning about nothing. As symbols are not real things, they are no-thing. There is no progress in logic. It is the process the mind uses; therefore it need not be taught. It is there in the mind as the process the mind uses to think.

I prefer to work with plants and to think about humans, which seems foolish, but that's the way it is. For example, one thing I have often wondered about is why most (not all) of the smells emanating from the plant world are experienced as a pleasant feeling, whereas the opposite is true for the smells emanating from the animal world. But "why" is not the right word with which to question nature. The small child often uses "why" in the sense of "tell me more." The adult uses "why" in the sense of "tell me your motives." "Why" is a word that applies only when two brains are communicating with the language of human speech. "Why" is a nonsense syllable in the system man uses to communicate with nature. This system is the scientific system. Don't ask why? Ask what it is? And think of it as things like chemical compounds or as a process involving molecules.

The word revolution is being applied right and left to the development of modern biological sciences—without justification in my opinion. Kuhn apparently started this custom with *The Nature of Scientific Revolutions,* which I once read with real pleasure. Kuhn has applied himself to the history of science by applying the scientific method of observation to the process whereby scientists arrive at concensus (4). His method is a welcome change from that of the philosopher-historians. But I have been surprised by the fact that many of my fellow scientists didn't seem to read Kuhn the way I did. Some of them wanted to claim kinship with Galileo every time they made a new discovery.

New discoveries are very nice things, everybody is happy, progress is great, business is good, we are going to heaven fast. That's right. It is fun to make discoveries. But that is not the nature of revolutions. Revolutions hurt, because something we believed in has to be rejected. That's how you can tell the difference between a discovery and a revolution. If the molecular biologists want a big word to describe a big thing—the surge of new information in the field of genetics and cell differentiation—let them use the word explosion.

The basic premise of biology—that it can be understood in the terms of the physical sciences—has in no way been altered by the molecular biologists. Nevertheless, modern biology has given us a deep sense of kinship with all living things. Molecular biology is the Saint Francis of the sciences. I used to think that speculation about the course of evolution was pointless because it was impossible to duplicate the process. But if the nucleic acids carry within themselves the records of their origins, as Eigen suggests, then we may in fact be able to deduce the chemical course of our origins from dust. The prospect is wonderfully exciting. I regret being born too soon.

But this basic assumption of the biological sciences that all biological phenomena can be explained in terms of the laws of physics and chemistry doesn't always seem to apply. The mind-body problem defies such an explanation. Our awareness, our consciousness, our capacity for thought reflect complex chemical processes occurring in our brains. Free will implies a capacity to control these chemical events—albeit to a limited extent. We cannot deduce the experience of consciousness from physical and chemical laws. At this level, biology endows chemistry and physics with a new set of properties.

Mind is not a real thing, but a different entity, associated in a curious relationship with processes in which only things are involved. The natural scientist can examine the things involved and note their correlation with subjective phenomena.

The scientific method cannot answer all our questions. We insist on raising senseless questions. We want purpose and design in the universe. Our notions of purpose and design are based only on our own built-in natural drives.

THE SERIOUS AND THE NOT-SO-SERIOUS

I appreciate the logic of the theologians who said, "God's name is secret." But they weren't theologians as defenders of dogma. They were searchers for truth. I cannot subscribe to any dogma. I consider myself religious, but many religious people wouldn't. Man is an animal, endowed with a brain that tells him he is going to end in Nirvana, and the same brain gives man a set of drives that makes him fight his own extinction with all his might. This is the human dilemma. The great religions provide comfort by either telling us there isn't such a place as Nirvana, there is a Heaven and a Hell, or by telling us that Nirvana is really very pleasant, which comes out in a curious sense to the same thing. The "Hell" of the Christian is the "Rebirth" of Buddhism.

I believe that the best thing a human being can do is to try to increase understanding of the entire reality—the all—around us. This can only be done by the techniques of the natural sciences. One can't figure it out by meditation. One must observe nature. In this sense, the natural scientist isn't creative at all. Perhaps this word should be applied only to the artist. Still, there is an aspect of the work of the scientist that is very similar to the work of the artist. The scientist puts questions to nature and nature answers. No speck of imagination here. The art comes in the process of figuring out how to put the questions, and the thrill comes when you get the answer—the thrill is the *signal* that tells you you have the right answer.

I enjoy great literature. There are passages in Shakespeare and the Bible that have moved me in a way impossible to describe. One has to be in the mood for that kind of reading, and one's taste changes with circumstances, so I can't tell what my favorite passages are. It might be this one this week and next month it will be another one. I like fiction that can be read with several layers of meaning, but I have never been able to wade through Joyce's monumental later work. I don't like nonsense. I cannot understand that anyone can be interested in the meaning of symbols that represent nonsense.

Ariel's song is a sample of the kind of poetry that gives me the same kind of thrill as the thrill of scientific discovery.

Full fathom five thy father lies;
Of his bones are coral made;
Those are pearls that were his eyes;
Nothing of him that doth fade
But does suffer a sea-change
Into something rich and strange.
Sea-nymphs hourly ring his knell:
Burden. Ding-dong.
Hark! now I hear them—Ding-dong
bell.

Ariel's song—The Tempest (Shakespeare)

The above lines may have been inspired by the exhilarating excitement of the naval explorations of Elizabethan England, but they can be applied equally to describe the excitement of scientific discovery. The scientists aren't taking the mystery out of life. Even if they wanted to, they couldn't do it.

I have borrowed the title of this article from a book by Barbra Ring, a Norwegian novelist and newspaper woman who was born in my home town, Kristiansand, a good many years before I was. After getting a divorce from an insanely jealous husband, she made her living by writing. She provided the original version of my favorite Kjutta joke. Kjutta, I must explain, was once a real character who lived in Kristiansand, but he has become a legend there in the form of a hundred varieties of Kjutta stories.

Kjutta was in a fight and was beaten up. He is describing the fight: "First, I hauled off and slammed him on the nose and didn't hit him, so I slammed him again the same way. Then he began to run, but I got ahead of him."

Literature Cited

1. Bentley, R. 1978. Ogston and the development of prochirality theory. *Nature* 276:673–76
2. Krebs, H. A. 1974. The discovery of carbon dioxide fixation in mammalian tissues. *Mol. Cell. Biochem.* 5:79–94
3. Krebs, H., Mitarbeit von Schmid, R. 1979. *Otto Warburg: Zellphysiologe—Biochemiker—Mediziner,* 1883–1970. Stuttgart: Wissenschaftliche Verlagsgesellschaft. 168 pp.
4. Kuhn, T. S. 1977. *The Essential Tension.* Chicago/London: Univ. Chicago Press. 366 pp.
5. Nachmansohn, D. 1972. Biochemist y as part of my life. *Ann. Rev. Biochem.* 41:1–28
6. Vennesland, B. 1963. Review of *New Methods of Cell Physiology. Perspect. Biol. Med.* 6:385–88
7. Vennesland, B. 1974. Stereospecificity in biology. *Top. Curr. Chem.* 48:39–65
8. You, K. S., Arnold, L. J. Jr., Allison, W. S., Kaplan, N. O. 1978. Enzyme stereospecificities for nicotinamide nucleotides. *Trends Biochem. Sci.* 3:265–68