Archives of Insect Biochemistry and Physiology 37:1–7 (1998)

For the Fun of Science:
A Discussion With John E. Casida

Bruce D. Hammock* and Kati F. Casida

The laboratory of John Casida has made major contributions to the field of insecticide biochemistry and toxicology for over 40 years. During that time he has trained numerous graduate students and postgraduate fellows as well as developed interactions with the major laboratories in the field. Thus, a meeting of the alumni of the Environmental Chemistry and Toxicology Laboratory brings together a large group representing much of the field of insecticide toxicology. There are few areas of insect biochemistry and toxicology not influenced by some of the over 600 research papers and books and 30 patents from Professor Casida's laboratory. Approximately 200 alumni of his laboratory hold responsible positions in many related fields. Some of these scientists are involved in the insect-related work which is so close to Professor Casida's heart, and this volume contains research papers collected in his honor. Of course, these papers come from only a small group of colleagues who were in a position to publish on appropriate topics in the time frame of the special issue of the journal.

It is very difficult to categorize the research of John Casida. Possibly it is best to refer to him as a scientist who transcends disciplines in search of solutions to interesting problems. Contributions have been made to pharmacology, environmental science, spectroscopy, synthesis, genetics, herbicide research, and many other fields, both in the generation of new knowledge and in the development of technologies and approaches valuable in numerous areas. Research on natural and synthetic pesticides in his laboratory has laid the foundation for more selective compounds of greater safety to humans and to the environment. Biochemical studies have defined the mechanism of action of many compounds in both target and nontarget species. There is a theme of the biochemical basis of selective toxicity of pesticides throughout his research. However, there are numerous orthogonal contributions extending from this theme into many other fields.

Research from the laboratory of John Casida covers diverse areas. Simply scanning the titles of the laboratory's bibliography gives the impression of a broad, if not random, series of problems being solved. However, a closer inspection demonstrates that the laboratory continually has moved from one strength to another. One can follow a line of science from the research at the University of Wisconsin on organophosphate insecticides through mechanistic studies on the gamma-aminobutyric acid (GABA)–gated chloride channel. Intermediate steps along this line of research included investigation on the mechanism by which animals activate the proinsecticides containing a phosphorus-sulfur bond to the corresponding phosphate. A fortuitous discovery in this project led to the recognition of highly toxic caged phosphates. These chemicals provided a cautionary tale for human safety, since related and highly toxic compounds were generated in the use of some fire retardants. Chemical investigations in this series have led to promising new candidate insecticides as well as useful ligands for studying receptors. These ligands, coupled with a study of the mechanism of action of caged phosphates, led to fundamental discoveries on the GABA binding site, an understanding of the mechanism of action of numerous organochlorine pesticides, and a series of valuable probes useful in pharmaceutical research. This work typified many of the projects in John's laboratory, where intellectual excitement drives a project from one adventure to another along a multidimensional path. Of

*Correspondence to: Bruce D. Hammock, Department of Entomology, University of California, Riverside, CA 95616-8584.

© 1998 Wiley-Liss, Inc.

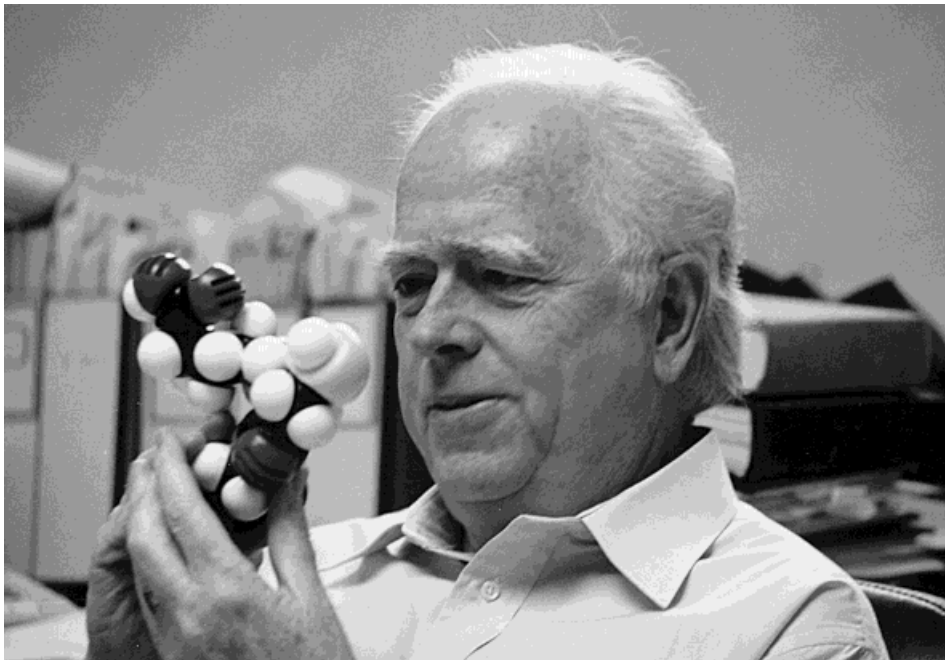

Fig. 1. John in his Berkeley office in 1996.

course, this project spanning decades was woven with numerous other interesting and occasionally overlapping lines of research.

A strength in a series of compounds, such as the pyrethroids, allowed the laboratory to develop programs in metabolic chemistry, radiosynthesis, neurophysiology, receptor binding, synergism, and other fields. An expertise with receptors and natural products permitted investigations on the mechanism of action of a variety of pharmacologically active materials in plants and animals using techniques such as affinity chromatography and photoaffinity labeling. Through this process John Casida appears a master in defining problems whose time has come for solution and in introducing new scientists in his laboratory to problems that will bring out the best of their scientific skills. At the same time, he drives the lab to continually be the first to contribute to a new field, which benefits both the lab and the individual scientists involved.

If there is a single trait which dominates John Casida's scientific career, it is that he thoroughly enjoys what he is doing. His love of research drives him and infects those around him. Recognition, financial gain, and other drivers seem insignificant in the light of the sheer pleasure of science. One of his more notable exploits involved arriving at the church moments before his wedding and, while waiting to approach the alter, being asked, "Where is Kati's mother?" Suddenly John realized that he had forgotten to pick her up at the hotel, and someone was dispatched at once to get her. She entered the church with only one comment: "Absent-minded professor!"

John Casida is very loyal, and, if he promises to give a lecture, he will give it. An example of this was a lecture he presented in India, on the day his second son was to be born. Happily, Eric understood his Dad and waited to enter the world until after John returned from India to Madison. On another occasion, John was so eager to present a lecture (or again so absent-minded) that he went a day early by mistake.

John has had a long tradition of making up for coming into the lab early by staying in the lab late. He gives endless hours helping with the wording and writing of papers and PhD theses. His wife, Kati, reports that the intensity of his research has never faltered to the extent that he will wake up at 2 or 3 in the morning and exclaims, "I have the solution, and the answer is so simple! I don't know why I didn't see it before." Of course, she wonders why he did not see it during normal working hours.

Members of his laboratory occupy leading positions in industry, government, and academics in many countries. Even when John is not at a scientific meeting, alumni from his laboratory congregate to discuss science, relive the experi-

ences from John's laboratory, and muse over what will be the next laboratory Christmas card that he and Kati devise.

It would be valuable if, from an examination of the career of John Casida, one could elucidate the recipe for creativity and productivity that still emanates from the basement of Wellman Hall. This certainly is too much to hope for, but some sparkle of his love of science and life may arise from his own words from a discussion in his office in August of 1996.

INTERVIEW

What got you interested in science?

I lived next to an arboretum and escaped there as often as possible. By the time I started high school, I was working in a lab 2 or 3 hours per day, and this increased to 4 hours a day at the University. It was during the Second World War, when jobs were readily available. You could focus on working in a lab and having fun with research. During this time I was collecting insects and interested in plants. That is the entomology bit.

Did your parents have a large influence on your interest in science?

Yes, by giving me freedom, and of course as role models.

Did your father seem to enjoy his work?

Very definitely. He had a strong influence on me. He was trained as a geneticist and reproductive physiologist. He instilled the idea into me that you need to do it yourself and follow through. You need to keep at it, and if you get away from science for a period of time (such as an administrator), it is very difficult to keep at the forefront.

Your brother is also a scientist?

Yes, a professor at Penn State in bacteriology.

Do you discuss your respective disciplines?

We often discuss bioactivity, particularly the chemical aspects. He is retired so that he has the option to spend full time on research.

Did you find your undergraduate times fun?

While working on my BS, I spent as much time as possible in the laboratory, doing both biochemistry and entomology. Classes were just well, a part of the game. My education was in the laboratory. I did a lot of fencing during this time as a release. This was my exercise for about 90 minutes a day.

When we try to reduce the cost of higher education by reducing laboratory classes, are we doing a disservice to our students?

It is more and more difficult to provide students with the stimulation they need in experimental science. Many of the laboratory courses are cut and dried and have to be finished in 2 hours or something like that. It is much more important that students work in a laboratory that is doing real research. If there is a way of expanding that opportunity, it would be a very good investment for society, the nation, the Republican Party, or whatever scale you want.

An editorial lamented in Chemical and Engineering News *the fact that the average MIT engineer knows far more about history, literature, and the arts than the average liberal-arts graduate knows about science. Do you see this trend towards the scientifically illiterate college graduate as a problem in undergraduate programs?*

I think curiosity should make one want to open up as much as possible to all disciplines. The opportunity to explore other classes outside of science as an undergraduate is important. But as science becomes more competitive and specialized, one may lose out on the breadth. Each person makes their own choices. You must be able to focus if you are to accomplish anything of meaning. Yet breadth is the richness of life. So how do you fit all of the disciplines in? Each person has their own routine.

With being married to a person who is quite a famous artist, how would you rate the value of an appreciation of art and literature to a young scientist?

I was fortunate to marry someone quite different in approach. So that interaction in my marriage helps to fill in for my wife, Kati, the science part and of course for me the art part.

Was graduate school fun or just more of the same undergraduate experience?

Graduate school was an opportunity to spend a higher percentage of my time in the lab. The classes were more focused and interesting, but there is nothing I love so much as working in a lab. Graduate school was interrupted after 2 years by some time in the Air Force during the Korean War. That turned out to be more research, so it wasn't so bad.

Do you see much difference in the graduate education you had vs. that we now provide students?

Graduate education depends on where you are and the flexibility of the place. My interests were between fields. At Wisconsin, a student could operate in an area that had not yet emerged as a discipline. It is easier to do that now at many institutions. Interdisciplinary education at the graduate level is more accepted. This is a good trend. One needs strong disciplines but also the free-

dom to move among disciplines and technologies. There should not be barriers between fields but instead channels to move between disciplines and thereby gain a more realistic feel for how science is going and is likely to develop in the future.

If you had the power to do so, would you change graduate education at Berkeley?

I don't think I'd make major changes. We should have graduate education accessible to as many students as possible from diverse backgrounds. However, there are the real problems of limitations of space and funding. As we discussed before, the freedom to explore and create in laboratories is so much more important than rote memory work in classes. The freedom to create must be integrated into any good graduate program, science or otherwise.

Your major professors gave you this opportunity to create?

I had three major professors. They were in entomology, where much of his work was applied in the field, in biochemistry with a fellow who synthesized warfarin, and in plant physiology with a specialist in auxin research. I had a lot of freedom since there was no one official area that defined my interest. I worked with insects and plants at organism and biochemical levels. My interests evolved toward a chemical-biological interface. I suppose that would now be insecticide toxicology.

Did you find it hard finishing graduate school?

Finishing graduate school was a matter of courses at various schools, some at Maryland while I was in the Air Force, coming back and turning in a thesis. I was appointed as an assistant professor as soon as I turned in a thesis. I guess the question was more about the ability to interface the degree work and the military service. The Korean War was winding down. There were some timing problems, but things worked out very well.

When you finished graduate school, did you find it hard getting started as an assistant professor?

There was not much funding to start with. A little from the experiment station. The university had a research foundation, WARF, that was the principal source of support. Certainly at Wisconsin WARF was a far more important factor than federal funds at that time. In 2 or 3 years, more funding started to come in. Funding for young scientists always is a critical issue.

What brought you to Berkeley?

I cannot imagine anyone resisting Berkeley. I have always appreciated the opportunity to join the staff here. I had taken all of my degrees from one place. I taught there for 10 years before I came to Berkeley. It was time that I moved on to something new. I did not feel inbred since I had worked in half a dozen different laboratories during that time. But it was a delight to come to Berkeley, and it has been a delight ever since.

The research that has come out of his laboratory would stand up well in any chemistry department in the nation as well as being the envy of many biochemistry departments. Yet you have been an entomologist for your career. Has this been a good home?

I am now in the Department of Environmental Science, Policy and Management but in the Division of Insect Biology. The location has never been a restriction for me. I should thank administrators for not making it a restriction. I have had wonderful colleagues in Entomology. It is a good home. We now are dealing with health-science issues that are pesticide related; pesticides are used as bioactive materials and probes to understand fundamental life processes.

What do you enjoy most about your work?

The wonderful opportunity to create, to follow your curiosity—that is, of course, if you have the resources. This is an important point of course for people entering the area. Following curiosity is one of the highest human endeavors and one of the most satisfying.

Do you have any advice for a person starting out in industrial or academic science?

Do something that you are interested in. If you are not interested in what you are doing, change fields. Try to find a location—government lab, university, industry, or whatever—where you have a chance to create, and you will be a success. Resources often are far better in industry, and the impact of your success is of a greater magnitude but somewhat obscured from the general public. It is often very hard to tell who created the major advances from industry.

Twenty-five years ago I asked you which project was the most exciting one you had been involved with. You told me, "The next project." Now if we eliminate the next project. . ."

Then it was the last one. At any one time in the lab we try to have each person on a different project and two or three people working in a general area. That area may be very broad, like natural products. We tend to have both biologists and chemists on a project. At any moment something can break. It's like the ag experiment station form that came out a few years ago. At the bottom is asked, "When do you expect your next big break-

through: 1–3 months, 3–6 months, 6–12 months?" If I did not expect something exciting to happen in the next 3 months, I would get out of the business.

Can you put a finger on what you think is the single most important contribution from this laboratory?

We try to teach a holistic approach; to follow the problem, not the discipline; to seek solutions, not always finding them; and most important, to create something new. That makes it sometimes difficult to write a grant application when you must say exactly what your approach will be. Rarely does one have the foresight when preparing a proposal on a problem that lets you follow through as you originally planned.

As a side step, we all are battling with the problem of acquiring funding to keep research operations going. The competition seems to force people to propose "sure" science rather than "high-risk" science. How do you deal with the knowledge that good science is high-risk science and the reality that such science is not funded so well as it once was?

In evaluating what we pick as subjects, I guess the primary questions are is it interesting and would it be fun to pursue. If we get excited about it, it is likely to be good science. Built into that process must be a consideration of the audience—for instance, the federal agencies that may fund it. You have to establish relevance, and that it is a good public investment.

I remember as a graduate student that you never told anyone to come in early or stay late, but you were so obviously having a wonderful time. There was this barely controlled excitement around you that it was easy to be in the lab at all hours. How have you maintained that over the years?

Just a great curiosity about what is going on. There are difficulties with one's own enthusiasm. One needs to convey a sense of excitement without generating pressure. One needs to provide suggestions and mention opportunities without giving orders. You need to give people in the lab space to create on their own.

How do you balance being enthusiastic without being overwhelming?

Often not very successfully and always a different way for each person. It's an interaction of personalities. When things work, the colleague will bring experience and ideas that I do not have, and I can contribute complementary knowledge. It's a blending of ideas. In this case, it is synergistic and catalytic, and there are no problems at all. There are times when our backgrounds are very close and we see things in a divergent way. This can lead to a new experimental design, and you work it out that way. I do believe in the results of the experiment determining the direction of the work.

A lot of scientists seem to start with an idea and then massage that idea for years. There are certainly themes of research that one can follow from your graduate-student days through projects that people are working on down the hall now. And yet more than any other laboratory in the field this lab has pioneered new ideas, started new areas, and moved from one strength to another. How have you managed that?

Thank you for your optimistic appraisal. Each person that comes to the lab starts a new problem. It may be related to a previous problem, but each person that leaves the lab may continue on the same problem, particularly if they move toward an academic job. Then the pressures of tenure dictate that they should not venture out too far from their experience. In starting a new problem, there always is constant debate of what areas to look at. It is rarely decided ahead of time. The negotiations when a person joins the group concern what we both are excited about and what backgrounds do we have that are complementary. We find something that we both would like to work on together. That, of course, puts you in many many different areas.

So in a sense the direction of the laboratory is determined in part by the people who are attracted to the lab.

Officially it is dictated by NIH and that which is in the grant application. The agency sets our long-term goals, and we work within those confines. In practice, the people in the lab create the environment for the research. They create the fun. You follow the problem, and it's the people in the lab that make that happen. If something is totally unexplainable and totally unanticipated, if it approaches the absurd, this may be the best reason for dropping everything else and focusing on that. This situation has happened often enough that I always look forward to it, but I never known when it is going to happen.

One of the characteristics of the lab is that you always invest a great deal of time in helping people to write their papers. You seem to savor every word that goes into the publications. What benefit do you get out of this?

I learn about the person and I learn about the subject. If it cannot be stated concisely and clearly, then the science is not properly under-

stood. The goal is to understand it if I want to tell someone else about it in writing. If my colleague is transmitting that information to the community, we want to make sure that it is clear, that the experiments can be repeated, and that my colleague feels the same.

I do not want to infringe upon your modesty, but there is no question that this is the most creative and productive laboratory in the field. What do you attribute this to?

To the extent your statement is true, success comes from people being in a relatively open environment that allows them to interact with each other. When you have 20 or so people representing many different disciplines and backgrounds, and you can keep them from being jealous of each other's accomplishments, then each person can create and interact with others in the laboratory, and to a certain extent you can sit back and watch what happens and enjoy it. But then you must wrap up the research to make it fit into the topics of the grant.

If we look over the last 30 years or so in pesticide chemistry, what major events have determined the course of the field?

A major event occurs when a new type of compound is discovered, when a new mode of action is elucidated, when we find a new metabolic pathway, a new way of integrating pest management, or a new resistance mechanism. Any one of these advances changes not only the immediate topic but everything that surrounds it. Other factors are the economics and the internationalization of science.

If we are trying to look ahead in the field, are there trends that you think are exciting?

The rush of knowledge that can be applied to a problem is fascinating and stimulating; you can't help but want to get more and more involved in different aspects of it. When you can get a crystal structure on acetylcholinesterase, you can ponder at a new level how this enzyme turns over its substrate so rapidly. Take a toxicant with a totally unknown mechanism, label it, photolabel it, find a receptor, sequence it, get a gene out, and test its biological relevance. It's so exciting to start with a total unknown and with an almost predictable sequence of how you will solve the problem, carry out the full routine of the science. Of course, the greatest kick when you find something totally unexpected.

If we look outside of pesticide chemistry and biochemistry, what are you finding most entertaining these days?

The increasing eagerness of the public to understand science as it affects their lives. This is best exemplified by any new findings on AIDS, but insect natural history, pesticide hazards, and many other topics are easy to popularize.

In an editorial in Science, *Dan Koshland said that the role of a professor has evolved from being a scientist to feeding his graduate student's children. In this context, how do you manage dealing with funding agencies, university bureaucracies, and other distractions vs. the time to be creative, time to read the literature, time with people in your own lab?*

I have always been fortunate to have colleagues that interacted in various ways with the program here—interacting to help keep it legal, financially sound, and scientifically correct in multiple disciplines. I guess I have not worried too much about how it was going to continue because there are so many things to do that one does not have time to think about that. You try to keep the problems that you are on moving and assume that, if productive, the research can be perpetuated. What is difficult, as I alluded to before, is something which appears as a serendipitous observation; this is often the most difficult to justify researching. We had on occasion research funding turned off on such problems because it is not what we said we were going to do but turned back on at a later time because it was the most exciting thing we had found. It's the unexpected breaks that make science most exciting. One hopes you will be able to get the resources to develop the new breaks.

Earlier you found release practicing with a saber. Are there hobbies that you have now?

Some photography. I go to Greece whenever possible. Archeology interests me. I enjoy dancing and Kati's career in art. I have many releases.

How important is it to have a life outside of science?

It's highly individualistic. I could drop into the lab and enjoy 2 weeks with interruptions from no one. There are so many things that I want to check on. The problem is how do you balance it. As Kati would clearly verify, when she is gone I live in the lab. When she is here I have a different sort of life.

Things must have gone right at home since both of your sons were attracted to technical careers.

They both became interested in mathematics at a level which neither Kati nor I can fully comprehend; perhaps they were escaping our directions.

When you are running a large laboratory

with all of its problems along with keeping funding coming in and administrators at bay, how were you able to go home and convey to your boys your enjoyment of science?

I think that they saw that I was enjoying it. They probably thought that I spent far too much time on it. Both of my boys went into more mathematical and less lab aspects—certainly this holds for the one who is a theoretical chemist. The other one went into microwave engineering. However, they both see that you have to keep a focus on your work if you are going to contribute. I enjoyed having a chance to follow through on a project, and I think that they enjoy this also.

Are there problems that you see in the scientific community?

It was relatively easy to move into a research career a few years ago. This is becoming increasingly difficult. There are more and more people in a postdoctoral holding pattern—moving from early to late twenties, early thirties, and on. Often these are extremely skilled and very creative people. Society does not provide them the outlet to really make a contribution except within the context of this temporary lifestyle. One of the greatest difficulties that I see is a system where people have so much to offer, yet the finances, economics, and to a large extent the priorities of society do not allow them to experience the joy in science that I have had.

Do you agree then with Dr. Vargas that we have overtrained in the sciences?

In the area of my interest, I would say definitely not, in the sense that we are dealing between biology and chemistry; you can move in either direction. This interdisciplinary field is the basis for so much of the life sciences. Many of the chemical and physical sciences also are moving towards this interface. Possibly rather than overtraining we should address proper training in the sciences.

Not only do we commonly not have enough resources in science, but those resources often are of the lowest priority. Agencies will fund science if they have a little money left over at the end of the year; universities will hire lecturers and postdoctorals but not assistant professors; industry will issue contracts but not hire a professional. Do you see a way we can use the resources that we have yet provide an attractive career for people who want to go into creative science?

To me the opportunities are there for a research career, but more and more guidance is needed in creating a personal science identity. I hate to differentiate areas of science that are popular and fundable vs. unconventional and poorly funded. Fortunately, the scope of funding is usually related to the quality of the science.

Years ago Kingman Brewster at Yale pointed out that the worst problem that occurs when we have an apparent lack of money for creative endeavor, whether science, art, or other disciplines, is that the very best people are driven from the field. Do you see that happening with repeated reports that young scientists are having trouble finding permanent positions?

Certainly a lot of people are driven away from the field. However, many others have a basic curiosity, and they will find the way to express it in science. Openings come in forms that one does not anticipate and certainly in structures of entrepreneurial start-up companies and joint ventures that I would have thought inconceivable not too many years back. I have never had a colleague in this laboratory with basic curiosity and drive and confidence in themselves who has not found a satisfying research career. In spite of many difficulties in our field, it still is a wonderful home for a creative person who wants to follow exciting problems.