

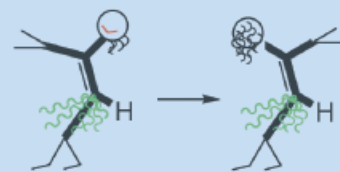
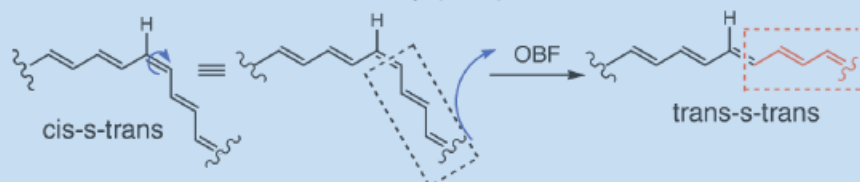
The Spectrum

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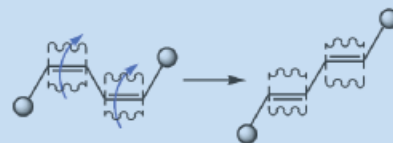
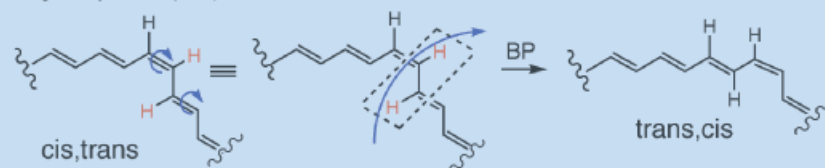
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Photoisomerization Reaction Mechanisms

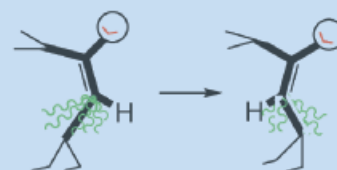
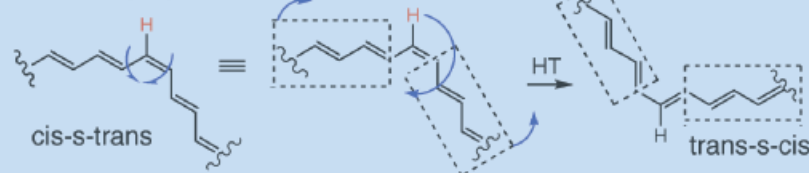
Torsional relaxation or one-bond-flip (OBF)



Bicycle-pedal (BP)



Hula-twist (HT)



Photochemistry
in the Middle of
an Ocean

An Interview
with Robert Liu

photochemistry in the middle of an ocean

an interview with Robert S. H. Liu

Be it resolved, that the House of Representatives of the Fourteenth Legislature of the State of Hawaii, Regular Session of 1988, commends Dr. Robert S. H. Liu for his excellence in teaching, his outstanding accomplishments in organic chemical research, and his overall contribution to science and the advancement of knowledge.

House of Representatives, State of Hawaii



Courtesy of Bob Liu

The University of Hawaii at Manoa launched a special lecture series a few years ago, with top faculty members making lunch-time presentations to the downtown business community. Those elite professors picked flashy titles to grab the attention of non-scientists.

One Egyptologist who used ancient mummies to study life and health in ancient times chose: "Mummy Talks: The Egyptian Mummy Project." A women's studies professor topped that with "Princess Di of the North" for her reassessment of Catherine the Great's role in Russia. One chemistry professor, however, took the cake with "Can Dogs See Ghosts?"

Perhaps more than any other photoscientist today, Robert S. H. Liu may be uniquely qualified to tackle that question.

Many researchers have delved into the basic chemistry of vision, arguably the most important human sense. Harvard biochemist George Wald, who won the 1967 Nobel Prize, spent a career on the topic. Bob Liu may be the only research photoscientist who devoted his professional life to vision at the most fundamental level. His work has been significant, involving highly unstable compounds that are horrendously difficult to separate, yet has received all-too-little attention.

Such may be the fate of a scientist on an isolated archipelago in the middle of the Pacific Ocean.

For more than three decades, Liu has focused on vitamin A (retinol) and the visual pigment rhodopsin. Rhodopsin is a protein in the membrane of the rod photoreceptor cells in the retina of the eye that catalyzes the only light-sensitive step in vision. It consists of the protein, opsin, linked to 11-cis retinal (formed after the body oxidizes retinol to an aldehyde). When photons strike the retina, retinal changes from the 11-cis form to the all-trans form. It triggers a chain of events that results in transmission of impulses through the optic nerve to the brain.

Liu worked with Ramamurthy to synthesize the previously unknown 7-cis isomers of retinal, the visual chromophore. During a sabbatical in George Wald's lab, Liu succeeded for the first time in binding several of the 7-cis isomers to opsin. He later did pioneering research on the binding site requirements of rhodopsin and bacteriorhodopsin, using an ingenious series of retinal analogs as probes.

The "Hula Twist" mechanism of photoisomerization, of course, is among Liu's other contributions, which he has reported in more than 220 papers. Bob tells colleagues that he is especially proud of four of those publications. They appear in the *Journal of Chemical Education*, and reflect how he teaches introductory organic chemistry courses, which are invariably over-subscribed. Noted on campus for putting on a good show, Bob sometimes lectures in a Superchemist shirt, or a Mandarin outfit—perfect for using Chinese noodles to demonstrate polymerization. How can you help students understand the polarizability of atoms? Bob compares it to body features of Konishiki, a gargantuan sumo wrestler famous throughout Hawaii.

Liu received an undergraduate degree from Howard Payne College and Ph.D. from Caltech under George Hammond. He spent four years in the Central Research Department at E. I. duPont de Nemours, where Bob modestly cites two major achievements: Discovery of the role of the second triplet state in photochemistry and convincing Regina Ro to become Mrs. Robert Liu. In 1968, he joined the University of Hawaii. He has been an Alfred P. Sloan Fellow, a John Simon Guggenheim Fellow, and received the University of Hawaii Regents' medals for excellence in research and in teaching.

Bob was born in 1938 in Shanghai, China, into a westernized family. Both grandfathers were officials in Chinese embassies in Europe. Bob's father got a master's degree in banking in the United States and his mother learned to speak French and English before she learned how to write in Chinese. As the Communists took control after World War II, the Liu family fled to Hong Kong.

In this interview, Bob reflects on his youth, initiation into the "Hammond Mafia," transitions into industry and

back, and research leading to the the Hula Twist. Liu notes that his research does suggest ways to improve human vision, and discusses other milestones in an extraordinary career in the photosciences. Bob even reveals how he got George Hammond to do the Hula Twist in Aloha.

The Spectrum: How did high school in Hong Kong lead to Howard Payne College in Texas?

Robert Liu: There was nothing logical about it. It was a matter of necessity. Howard Payne was the only college that gave me sufficient financial assistance—a small scholarship and a guarantee of a sizable workshop.

The Spectrum: What did you think when you arrived in Brownwood, Texas—a foreign student in a small town?

Liu: Brownwood was a town of 10,000 in tumbleweed country, without a single Chinese restaurant. In fact, when I walked downtown, I got the impression that people across the street whispered, “Look! A yellow face!” I had no time for culture shock. After paying the immediate required items on registration day, the \$250 in my pocket had dwindled to \$54. Nothing more was going to come from my parents. I immediately signed on to work and to find any odd job on campus that fitted into my schedule. But no cash was paid for those jobs, only credit toward my expenses. I had to find odd jobs off campus for the minimum wage of \$1 an hour—double what the on-campus jobs paid. That seemed heavenly then.

The Spectrum: You majored in chemistry?

Liu: Dr. Daniels, the only chemistry professor at Howard Payne, convinced me to switch from chemical engineering to chemistry. In the first place, there was no engineering of any sort offered at HPC. Also, Dr. Daniels himself had switched from chemical engineering to chemistry when he was a student.

The Spectrum: How did you find your way to George Hammond?

Liu: Caltech was the obvious pie-in-the-sky for me. In Hong Kong, Caltech was known as the MIT of the west. My

first two quarters at Caltech were sheer panic. Everyone in my class seemed to know so much more and had wide ranges of research experience. My only “research experience” was reading Werner’s book and review articles on coordination chemistry. I took the intermediate organic chemistry class taught by George Hammond. I was so impressed by the fact that there was logical, deductive reasoning in organic chemistry rather than all brutal memorization. And I also heard through the grapevine that his research group was doing exciting new things. So, I asked to be a member in his group. I knew it must have been a surprise to him because I was supposed to be an inorganic chemist. George had just accepted three new Ivy leaguers into his group. One more person from Timbuktu could not possibly

be a welcome addition. But he put on a pretty good poker face and said yes.

The Spectrum: Who was there in 1961?

Liu: Angelo Lamola was the obvious star student in my year. He already had five or six papers on his record and seemed to know everything. Ahead of us were two other stars: Nick Turro and Jack Saltiel. All three helped me greatly in my early venture into research. I learned every basic photochemical technique from Nick. From Angelo I learned how to do independent research. At first, when I ran into a blank wall, I waited for the next opportunity to talk to the master.

Angelo would tell me not to wait for words from the top but rather to keep on trying on my own. Soon, I stumbled across the gold mine of photosensitized dimerization of isoprene. Jack showed me the need to be thorough in one’s thought process. His stilbene work was simply trail-blazing and no doubt, he was sharp and imposing especially to a dumb first year student. But Jack, at that time, also had the habit of reminding you, “How stupid can you be!” At least I had enough sense not to fold in front of him, but rather learned to be more thorough in my thought process.

The Spectrum: Why isoprene dimerization?

Liu: It was an ideal project for a starter. At first, it was a challenging separation problem when I obtained a mixture of seven dimers. Then it became a learning experience to assign all seven dimers using primarily NMR spectra with



Bob with George Hammond at an outing at an IAPS meeting in Iguazu Brazil.

Courtesy of Bob Liu

a 60 MHz spectrometer. It was also an analytical problem to obtain quantitative numbers of dimer composition as I changed the triplet photosensitizers. Toward the end of the first summer, I typed out my first progress report for George, 35 pages long. I remembered it was in red because only the red ribbon on the typewriter in the lab was any good. I turned in the report on a Friday.

The Spectrum: And probably held your breath all weekend.

Liu: Monday morning George charged into my lab with that silly grin on his face. He started to tell me the idea about stereoisomeric triplets of conjugated dienes, how the rapidly interconverting ground state conformers of the dienes becoming non-interconvertible isomeric triplets in the excited state and how the relative amounts of the isomeric triplets varied depending on the triplet excitation energy of the sensitizer. It was non-stop talking for 10-15 minutes from a very excited boss. The following day, in the library I found a paper by Evans on singlet-triplet absorption spectra under high pressure of oxygen. In it was the triplet excitation energy of transoid butadiene (60 kcal/mole) which was indeed higher than the cisoid 1,3-cyclohexadiene (53 kcal/mole)—the needed hard evidence for George's postulate. I happily showed those numbers to George.

The Spectrum: George seldom wasted time getting a discovery into print.

Liu: The next Friday, George visited my lab again to show me a hand-written copy of a communication intended for JACS with me being the sole co-author. Even though during the library search I began to understand some of the significance of the work, I was still surprised by the quick turn of events. Could it be right that this very green student, still unsure of his future, would have a paper in his first year of study? I began to entertain the thought that they might not flunk me out after all!

The Spectrum: You certainly joined an exceptional group of people destined to shape modern organic photochemistry.

Liu: That was a unique group of excited graduate students. We learned from each other, grilled each other, but we never got mad at each other. We were the hardest working group, but we never felt that we were working. George never was over-bearing but we all knew that he was a big part of the

success. And the research program itself had a lot to do with the unusual atmosphere that existed. I don't think any of the original Hammond Mafia nor anyone else was able to fully reproduce that atmosphere when we later established our own research groups.

The Spectrum: What did you learn from George and the rest of the group that proved most important later on?

Liu: The episode of isomeric diene triplets showed me George's uncanny ability to grasp the central point of a narrow experimental observation and generalize it into a concept of broad impact. George never taught us how to do experiments, but he showed us how to think. I learned by watching and listening to George's reactions in Monday night seminars and I relished the opportunities to listen to him talk about our work to a general audience. Suddenly, it seemed that without my work on photodimerization of isoprene, the world would be poorer in our understanding of radiationless transitions of electronically excited molecules. I am sure some of the generalizations turned out to be mostly bull later on. But, oh! It felt so good listening to him. And that ability to generalize is something I always tried to imitate when I was on my own.

The Spectrum: And that first paper led you forward.

Liu: The isoprene project was the beginning of a rather involved investigation of chemical properties of diene triplets in general. I wanted to collect and synthesize every diene that came into my mind in order to examine their triplet chemistry. The next two years of my stay in Caltech were the most enjoyable years of my life.

The Spectrum: What attracted you to DuPont?

Liu: Partly, necessity. During my final year at Caltech, my father suffered a debilitating stroke. I felt obligated to contribute to the financial need facing our family. So, I spurned the chance to postdoc in Paul Bartlett's lab and took an industrial job instead. I was lucky to be on the last leg of the CRD philosophy that publication in first rate journals was good for the company. I worked under Howard Simmons, the top organic chemist there, who gave me a free hand to do what I considered important. I spent four years there.

The Spectrum: Was it common then for new CRD chemists to make a career decision after three to five years—to stay or test the waters in academe?

Liu: I belonged to the second group. When I told George, he mentioned that there was an opening in Hawaii that would be ideal for me. Hawaii turned out to be the only place that offered me a position and it was an associate professor position. Even at that level, I had to take a 30% cut in salary. But I was eager to try out the academic life. So, with my new bride, we packed up and moved west, way west.

The Spectrum: Was there any concern about isolation due to the distance from the mainland?

Liu: Perhaps isolation was a problem. But I think I used it to my advantage. I never considered myself very good in competing in popular areas of research. Instead, I often worked in areas that were of little interest to others. For the T_2 project, I used to comment that quantum yields were so low ($<10^{-3}$) that any academician would perish long before finding any interesting results to publish. As an industrial chemist, I never felt the need to rush things. Even later on when my group became known for the vitamin A work, people wondered why I continued to work in such a difficult area with highly unstable and difficult-to-separate compounds. I did not mind the loneliness as we plodded slowly ahead.



With V. Ramamurthy in front of Bilger Hall, the chemistry building at the University of Hawaii.

Courtesy of Bob Liu

The Spectrum: You did sabbaticals with two Nobel laureates, George Wald and George Porter. What are your recollections of Wald, who became quite controversial as a political activist, and Lord Porter?

Liu: When I joined George Wald's group, he already acquired many outside interests and devoted only a fraction

of his time in the lab. Only on one occasion, he called me over to help him inject vitamin A into bullfrogs for his study of A1 to A2 conversion. I am not a politically minded person. We never discussed his many political views while I was there. But I kept him informed of my progress in the lab. When the time came for me to prepare a draft for our first paper on isomeric rhodopsin analogs, I naturally included Wald as a co-author. But he said, "No!" He read it and offered generous suggestions but he declined to be a co-author, saying that he was only a reader.

The Spectrum: And Lord Porter?

Liu: The environment at the Royal Institution when I joined George Porter was unique. He was the director, and a big part of that job involved presenting science to the general public. There were constantly groups of high school students marching in and out of the building. Thursday evenings were the usual black tie events attended by people from all walks of life, including royalties of the highest level. The presentation given by Porter himself in one evening while I was there was simply out of this world. What a showman! At 9 p.m. sharp, "Ding!" the main doors to the lecture hall opened and in came Professor Porter in splendid tails. At 10 p.m., "Ding!" Out went the Professor. In between there was a non-stop performance of at least 30 chemical demonstrations. I remembered telling myself that I must borrow a little bit of that flair and showmanship into my lectures.

The Spectrum: How did you start on the preparation of new stereoisomers of vitamin A?

Liu: In my third year at Hawaii, Ramamurthy came on board. He was a "mistreated" physical chemistry graduate student in India and decided to restart his graduate study in Hawaii. Quickly I noticed his drive and efficiency in some simple warm up project that I gave him. So I suggested that he should work on truncated vitamin A analogs, starting with dienes then working his way up to trienes, tetraenes and eventually with the pentaene vitamin A. In spite of his physical chemistry background, he immediately jumped in to synthesize all the starting materials needed for the photochemical studies.

The Spectrum: And he started on the ring-containing diene fragment of vitamin A?

Liu: Yes, β -ionol. In no time, he came back with a stunning result. Not only could he carry out the trans-to-cis

isomerization, but under the selective triplet sensitization condition he was able to achieve the conversion in 100%. Apparently “non-vertical” excitation was not an impediment in this case, even though it was known to divert stilbenes and piperlyenes away from quantitative trans to cis conversion. When I did a little literature research later on, I was surprised to find that such 7-cis geometry was unknown in the vitamin A and carotenoid field. In fact, in a 1939 paper Linus Pauling predicted that such 7-cis and even the less sterically hindered 11-cis isomers of vitamin A were too unstable for existence. No serious attempts were made to prepare olefins containing such a hindered geometry. The obvious conclusion was that Linus Pauling was simply too convincing. His paper must have dissuaded chemists from trying.

The Spectrum: Sounds like one case when people took the literature too seriously.

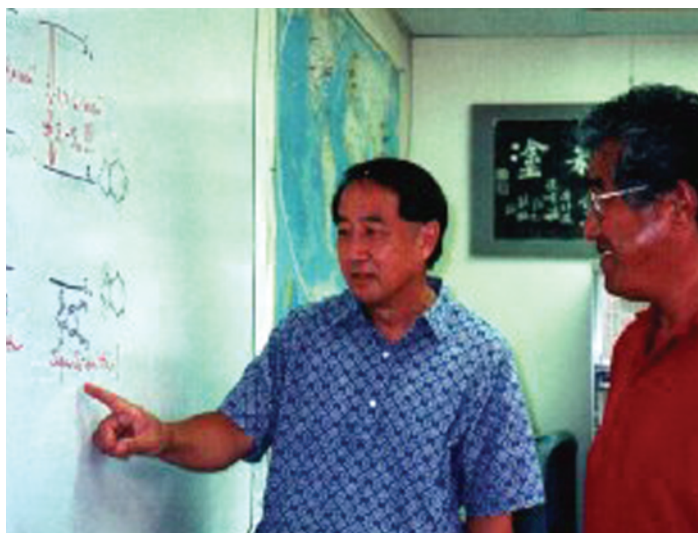
Liu: Yes, it seemed so, but we did not know better. And it was, no doubt, very reassuring when we had gram quantities of the 7-cis isomer sitting on our bench when we found out that they were not supposed to exist. Subsequently, Murthy demonstrated that the triene analogs also gave the 7-cis isomers in near quantitative yield. But the luck stopped there. Any longer polyenes failed to give a trace amount of the hindered 7-cis isomers. Soon, however, Ramamurthy departed for a postdoc position in Paul de Mayo’s lab. Before his departure he completed partially a total synthesis of four new isomers of vitamin A. I was able to convince the *Tetrahedron* editor that we had sufficient information to merit a paper in that journal.

The Spectrum: But your new synthetic adventure continued?

Liu: Thanks to a paper by Nakanishi on 14-methylretinal in *JACS* in which the use of a Corasil hplc column was

mentioned for isolating their retinal isomers. It was some hplc column, 7 feet long with 20 micron silica gel (finest particle available then). I duplicated the condition and tried it out on the only hplc unit in the department. At that moment I had no reliable student to work on this project, so I did all the work by myself. Walla. There were the 7-cis and 7,9-dicis isomers, all cleanly separated, with a partial separation of the two 13-cis isomers. Later I showed Murthy the 100 MHz H NMR spectra of the purified isomers. I think that was the only time Murthy thought that I was a competent experimentalist.

The Spectrum: Murthy’s work pointed you in a new direction.



Discussing with Al Asato, a long time associate, on azulenic chromophores.

Courtesy of Bob Liu

Liu: It demonstrated synthetic utility of a very efficient photochemical transformation, and opened the door to many new things for my group. I managed to create an assembly line for our budding bioorganic program: Synthesis by Al Asato, photoisomerization by Marlene Denny, protein analog studies by Hiro Matsumoto and paper writing by me. It was an efficient operation. With that jump start, I was able to line up several collaborative research groups to carry out more detailed biochemical and biophysical studies of the

rhodopsin analogs prepared in this laboratory. Along the way, I decided that there was a need to introduce methods of our own for examining protein substrate interactions particularly in cases like rhodopsin where the 3D protein structure was unknown. The crystal structure eventually came out in 2000. So, I decided to start our own molecular modeling and our own protein NMR studies using F-19 as the reporter. Eventually, we were armed with data to discuss topics such as stereospecificity of the binding site of rhodopsin and regiospecific protein perturbation on the retinyl chromophore in a more specific and somewhat more quantitative manner.

The Spectrum: Did the rhodopsin system focus your attention on isomerization within confined cavities and get you thinking about those hula dancers?

Liu: The Hula-twist, yes. When I was ready to reveal this new mechanistic process, I mischievously included the name Hula-twist (HT) in a footnote.

The Spectrum: And it jumped out and caught on...

Liu: The hula-twist was designed to answer an obvious question that arose in the mid-1970s about the photochemistry of rhodopsin: How can the very volume-demanding torsional relaxation process, the traditional mechanism for cis to trans isomerization, take place within the rigid binding cavity of rhodopsin? It was clearly a question on medium-directed photochemical reactivity asked before supramolecular photochemistry became popular among organic photochemists. Arieh Warshel first proposed the volume conserving Bicycle-Pedal mechanism of isomerization in which two alternating bonds rotate simultaneously. I found the idea fascinating because it was the type of conformational and mechanistic photochemical reasoning that I was supposed to know something about.

The Spectrum: How did you work it out?

Liu: With the help of a simple set of molecular models. I soon found a different mode of volume-conserving isomerization. Instead of rotating two alternating double bonds, if one rotates two adjacent bonds simultaneously, the same cis-to-trans isomerization can be achieved. For a conjugated system, this means rotating a double and a single bond. Hence, only the middle H-atom flips in-and-out of the plane of the molecule, obviously a volume conserving process. It has the advantage of isomerizing only one double bond. Therefore, it was not in conflict with the known one-photon-one-bond isomerization (11-cis to all-trans) of rhodopsin. The additional single bond isomerization would produce a high energy ground state molecule—that did not seem to be a problem because many dark intermediates of rhodopsin were known.

The Spectrum: So you had a mechanism. What about the supporting evidence?

Liu: It turned out to be difficult. Practically nothing happened during the next 13 years. It was not until 1998, a paper appeared in *Angew. Chem.* in which Werner Fuss and

coworkers described photoisomerization of pre-vitamin A in an organic glass at liquid nitrogen temperature showing simultaneous isomerization of a pair of adjacent double and single bonds, the expected stereochemical consequence for the HT process. Fuss kindly communicated with me before the paper appeared in print. This paper not only revived my own interest in the HT mechanism but also made it clear to me the exact conditions for finding new examples of HT. In the literature I found many “unexplained” photoisomerization examples conducted under confined media that could be successfully accounted for by the HT process. I decided that future studies should not be limited to my lab. So, I proceeded to lay out all my ideas in two papers in *Proceedings of the National Academy of Sciences* and *Accounts of Chemical Research*.

The Spectrum: The response?

Liu: Well, the world was not eager to pick up the island music and follow the HT beat. So, instead, I redirected my limited resources on the search of new examples of HT. Subsequently, a new source of money came from the National Science Foundation. Three consecutive postdoctoral researchers brought to fruition all the predicted examples of HT. Hula-twist as a viable photochemical reaction mechanism appears to be beyond doubt.

The Spectrum: Some chemists still don't hear the island music, do they?

Liu: Well, people tend to be comfortably stuck with the old tune. The traditional one-bond-flip, OBF (or torsional relaxation) mechanism of isomerization is deeply ingrained. The need to think about the HT-processes one vinyl hydrogen at a time seems to escape the minds of quite a few people (or deemed too complicated to others). I suspect that is because there is no equivalent regioselective OBF reactions that lead to uniquely different chemical consequences. But such mistakes are really not quite excusable for those who chose to march into this mechanistic project on their own while disregarding what have been clearly delineated in the literature.

The Spectrum: Tell us how you got George Hammond doing the hula twist in Aloha.

Liu: When I was completing the second HT paper in 2000, it became obvious that the theme overlapped with that of isomeric triplets of conjugated dienes. So, I searched for my

old boss, and found George was happily residing in the retirement community of—of all places—Aloha, Oregon! I told him about my project and invited him to be co-author. He responded positively within a week. So there it was: George started to gyrate the hula-twist in Aloha! That also turned out to be the start of another round of collaboration between George and myself. At this moment our fifth paper since the turn of this century just appeared in print. My first publication ever was published in 1963 with George. Forty-two years later I am again publishing with him. The only difference is that I have since boldly put my name in the front. Also, I can proudly brag in front of other ex-Hammond members about this record of longevity in joint publication with one's mentor. Hey, Dick Weiss, over there at Georgetown University! Can you beat that?



The Superchemists of Organic Chemistry II. Liu (middle) with his students.

Courtesy of Bob Liu

The Spectrum: Does research on the chemistry of vision have a sufficiently high priority at NIH?

Liu: I am glad you asked this question. The answer is not so clear cut. There is a National Eye Institute (NEI), one of the smallest institutes under NIH. My first two years of the NIH grant was picked up by NEI. But NEI is more interested in curing diseases of the eye. Instead, soon it became obvious that our bioorganic program had a broader impact than the visual process alone. The larger DK (Digestive Diseases and Kidney) Institute became interested in our findings and generously supported our research program for the next 26

years and in between the National Cancer Institute (NCI). They bought us some large preparative hplc instruments for scaling up of the new vitamin A isomers for cancer preventive studies. I guess the answer to your question is: for any long term support, one will have to be flexible.

The Spectrum: Then, NIH has been your primary source of support.

Liu: Our photochemistry program also received generous support from the Army Research Office (ARO) and the National Science Foundation (NSF). The ARO's interest was largely in the near infrared absorbing materials including non-linear optical materials and unusually long wavelength absorbing visual pigments and bacteriorhodopsin analogs. The NSF support allowed us to probe for information of excited state properties of polyenes without having to worry about their immediate applications.

The Spectrum: What's keeping you busy now?

Liu: HT launched us into thinking about other general photochemical issues such as how distribution of the ultrafast relaxation processes of the initially electronically excited molecules (the Franck-Condon species) can affect the eventual chemical fate of the molecule. Excited singlet state reactions of olefins are particularly rich in different relaxation pathways. It became clear to us that such ultrafast processes should be extremely sensitive to external perturbations including minor effects not normally considered important in perturbing chemical reactivity (of the thermalized excited species). Such thoughts necessitated a reorganization in my own mind of medium perturbation effects on trapped substrates. Supramolecular effects on protein bound substrates must be related to those effects already established for substrates trapped in many man-made host systems. While this is still a developing story, some new thoughts have come forward. For example, the supramolecular effects of organized hosts (crystals, zeolites or any other defined structures) can be very different from that of amorphous organic glasses. In organized hosts, the immediate space available for reactions could be larger than that encountered in solution, and reactivity may be less inhibited. But in an organic glass, the collapsing host molecules surrounding the substrate as the solution freezes mean less space, making the reactivity of the trapped molecule more inhibited than that in solution.

The Spectrum: Looking back on those 44 years in chemistry, what was the single most important key to success?

Liu: If there is one, it would be that I was quite lucky in having avoided any situation that required lengthy periods of professional training. Caltech allowed me to learn and produce simultaneously throughout the 38 months there. DuPont did not require postdoctoral training. I was green but I observed and learned how to navigate under a very capable boss while moving ahead on the scientific front. I even learned in the mandatory semiannual performance reviews that required me to justify continued support from upper management. It was a useful preparation for proposal writing. In Hawaii, I was spared the usual induction or observation period of an assistant professor. That trust perhaps only served to give me more confidence to learn and explore new projects as we moved along. I never felt that my relatively short period of formal training was a handicap in my later life. In fact, it might have worked the opposite way. My youthful exuberance, or naiveté, probably did lead to some mistakes. But it also opened the doors to new areas not visited by others.

***The Spectrum:* And the long training periods today?**

Liu: To me, they are excessive. They can easily stifle enthusiasm and motivation. I am therefore very supportive of the recent drive to shorten national postdoctoral fellowships to a maximum period of three years. Similarly, any program or policy to discourage Ph.D. tenure to six years or beyond should be applauded.

***The Spectrum:* Before closing we must ask whether your research really suggested routes to the kind of improved human vision you alluded to in that talk to the downtown business folks?**

Liu: I think you are sneakily baiting for the answer to the question: "Can dogs see ghosts?" Sorry, I am not going to let the cat out of the bag. By the way, I am hoping to take the show to the ACS Speaker Circuit. But I can tell you that after some discussion on the background information on the chemistry of vision, I did return and gave an answer to that very question. At the same time I also mentioned that we are on the hot trail of providing an answer to the question why the rhodopsin pigment is so much more sensitive than the same vitamin A chromophore in solution. It is a question that has puzzled researchers in the vision field for some time. The situation is identical to putting a roll of ASA 200 film into a magical camera and finding that it suddenly behaves like ASA 800, a four-fold increase in sensitivity. Understanding the mechanism of enhancement

of this magical camera is clearly very important. We believe that not only we have some understanding of the enhancement in our eyes but also with some defined fine-tuning (chemically), we might turn that roll of film into one of ASA 1200. Is that important research? I thought it was. But that was when my NIH program ran into an unceremonious termination. Apparently I had stepped on the sensitive toes of those controlling the purse string, those believing that no one could improve on Nature!

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