James F. Crow: Storied Teacher, Leader, and Colleague at the University of Wisconsin

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ALL told, the two of us knew James F. Crow for 105 years. Rayla Greenberg Temin received her Ph.D. in genetics in 1963 with Jim as her major professor. After receiving her degree, Rayla remained in Jim's lab for many years as a research scientist working in collaboration with Jim. In 1978 she became a member of the genetics faculty. She recently retired and continues to be active in genetics as an emerita professor. Millard Susman joined the genetics faculty in 1962 and is still affiliated with genetics as an emeritus professor. Our assignment is to describe Jim as colleague, teacher, mentor, and friend, and our challenge is to do that without straining the credulity of our readers. We have all known extraordinary people whose originality, productivity, and influence were many standard deviations above the mean but who may have had foibles and incivilities that seemed somehow to counterbalance their inordinate strengths. Not Jim Crow. He was one of those exceptions that we are taught to treasure.

In the spirit of Dr. Crow—a legendary raconteur—we relate some stories about Jim as a young scientist-scholar, about the intellectual life in Jim's lab, about his contributions to genetics education, and about his interactions with colleagues in science and beyond. We draw, to some extent, on Jim's writings about the history of genetics, including his own history, and on stories we heard from Jim himself. This article is one of a series of Perspectives pieces conceived as a celebration of Professor Crow in his 95th year. It is intended to be complementary to the previous two articles (Hartl 2011 and Abrahamson 2012). Professor Crow read, and greatly enjoyed, the published articles in this series. Sadly, he passed away on January 4, 2012, while this article was just beginning to take shape.

One of the keys to Jim's success was that, at the very beginning of his teaching career, he sought out and connected with his "heroes" in genetics, becoming lifelong friends with them. Although Jim was consistently mild mannered and modest, he was by no means shy; with his intuitive mind and his cheerful, gregarious nature, he quickly entered the circle

of leaders in genetics. While an assistant professor at Dartmouth (1941–1948), Jim made several trips to Amherst College to visit H. J. Muller, whose work he admired. He reported that his first meeting with Muller, in 1944 or '45, was "the only time in my life I was so excited about the various new ideas that I got from him that I didn't sleep at all that night" (Crow 2005). Then, in the summer of 1946, when Jim went to Raleigh, North Carolina, to take a course in statistics, he met R. A. Fisher, who gave a lecture on the inheritance of Rh factor, invoking his three-locus model. That meeting, with the help of a bottle of champagne, launched a lasting friendship (Crow 2000).

The next summer, thinking that nucleic acids were going to be important and that he should learn something about them, Jim attended the 1947 Symposium on Nucleic Acids and Nucleoproteins at Cold Spring Harbor. An evening talk became a turning point in Jim's life. It was given by Joshua Lederberg, who described his studies on recombination in *Escherichia coli* K-12 and his preliminary genetic map. Jim was fascinated, realizing the potential power of a selective system that made it possible to do the same kind of genetics in bacteria as in higher organisms. Jim asked several questions about linkage and the assumptions Josh made about interference; their conversations continued through the rest of the symposium. Lederberg, in a 1986 talk honoring Jim on his retirement, recalled that Jim was "one of the liveliest and best informed and engaged people at the (CSH) symposium. I came to Wisconsin as an assistant professor that fall, 1947. When a new position opened up the following year, that experience pointed to him as the most desirable of candidates, and indeed he was." Thus Jim's early perceptive interest in nucleic acids led to his meeting Lederberg, who brought Jim to the attention of the Genetics Department at Madison. Jim and Josh had adjacent labs and spoke every day; they remained close colleagues and friends throughout life and consulted each other on all manner of things. Thus, in 1996, when Josh wrote a letter to the editor of the New York Times expressing his concern over the future lethality of the flu, Jim e-mailed Josh, "Did I ever tell you that I am a survivor of the 1918 epidemic? We ought to be of some use, or at least our blood." Josh's riposte was "You must have been

2 or 3. Now, if you had only thought to put some sputum in a (anachronistic) freezer. I'm trying to promote a project to collaborate with Russians at Siberian cemeteries on that tack." Jim, with typical self-deprecation, seemed amused by the suggestion that he might have made a greater contribution to humankind if he had died at the age of two and been preserved in a freezer.

This self-deprecation was one of Jim's charms. Once, when Jim was Chair of Genetics, the Dean told him that he deserved a hefty pay raise. Jim demurred, pointing out that he was already well compensated and that there were several assistant professors in the department who needed a pay raise more than he did.

Crow's relatively small and crowded one-room lab in the late 1950s was an informal and bustling place, with a great deal of sharing going on; it was a pleasure to learn in such an atmosphere. Rayla joined the group as a graduate student soon after Motoo Kimura and Newt Morton had completed their degrees, when Jim, having initiated his research program at UW with his work on DDT resistance in *Drosophila*, shifted his focus to genetic loads: its theory and estimates. Morton, Crow, and Muller had published their classic 1956 paper (Morton *et al.* 1956) in which they used consanguinity data, mostly cousin marriages, to assess the amount of hidden genetic damage and, using equilibrium theory, to estimate the human mutation rate. Using a somewhat parallel approach Jim launched a major research project in *Drosophila* to assess the impact of mutation on population fitness—a 20-year series of experiments that stretched from the mid-'50s to the mid-'70s. In the early phase were studies to partition the homozygous viability load into lethal and detrimental loads, using flies from nature to determine whether the reduction in fitness with inbreeding and the effects of recurrent mutation were due mainly to a few genes of major effect or to the cumulative activity of a number of genes with individually small, even tiny effects (Greenberg and Crow 1960). Several studies were directed to measuring heterozygous effects of lethal and detrimental mutations (for example, Hiraizumi and Crow 1960; Maruyama and Crow 1975; Ohnishi 1977; Simmons *et al.* 1978; Temin 1978). The ultimate conclusion was that there is hardly ever a completely recessive gene, at least in *Drosophila*. Mukai performed a series of studies on the deleterious mutation rate and dominance of genes affecting viability (e.g., Mukai *et al.* 1972). It was in the course of the fitness research in the late 1950s that Hiraizumi discovered SD, segregation distorter (Hiraizumi *et al.* 1960), which provided a great deal of excitement to all of us in the lab, as we dutifully counted our flies. As a major professor, Jim provided sage guidance, oversight, and creative criticism, but he was always careful to give us the freedom to grow as independent scientists.

Jim and the group he directed helped to shape the field of genetics in many ways. One event, which may not be widely known outside of *Drosophila* genetics, is that the *Drosophila* Research Conferences originated in Jim's lab! As background, we note that Jim's lab was a Grand Central Station

Figure 1 James F. Crow, R. A. Fisher, and Motoo Kimura in the Crow lab in 1961.

for visiting luminaries and pioneers, including Haldane, Fisher, Sturtevant, Muller, and Wright (Figure 1). The privilege of basking in the intellectual climate created by these distinguished guests was one of the many benefits of being a Jim Crow student or colleague. We received a trio of visitors in the fall of 1958: Dan Lindsley, Bill Baker, and Ted Pittenger—friends of Jim and his postdoc Larry Sandler. For 2 whole days, the Crow lab—including Yuichiro Hiraizumi, Elaine Mange, Tom Gregg, and Rayla Greenberg—talked science with Jim and his visitors. In the words of Larry Sandler (Sandler 1981), this was just a small get-together that could have been called “genetic analysis for fun and recreation,” but it turned out to be the first *Drosophila* Conference. It was so much fun that it met again the next year, in Chicago, as the Midwestern *Drosophila* Conference, a casual gathering attended by 15–20. That meeting was fun too, but created a furor when other *Drosophilists* heard about it. Ed Novitski and H. J. Muller, for example, were outraged that they had not been invited; so, in 1960, there was a Third Annual *Drosophila* Conference, at Bloomington Indiana, open to all, and the meetings took off from there. At the 38th Conference, in 1997, Jim gave a historical perspective. Recalling the modest beginning in Madison, attended by about 10, and, ever the quantitative appraiser, Jim noted that “the organization has grown at an enormous rate. . . . But let me caution you that what is gratifying will become appalling if continued. Another 38 years would swell the membership to a quarter million. The exponential growth has to stop!”

Teaching was one of Jim's greatest strengths. His lectures in the classroom were rigorous, lucid, well organized, and entertaining. And you could tell how much he enjoyed lecturing. Both of us had the pleasure of teaching discussion sessions in Jim's General Genetics course and working with Jim on a variety of other teaching assignments. Years after taking his classes students remembered him as “the best professor I ever had.” On the first day of the semester, Jim took pictures of all the students in his large (over 200) class.

He carefully glued these mug shots into his gradebook so that he could learn the names of his students. It amazed them that he could call on them by name when they raised their hands to ask questions. We adopted this picture-taking practice in our own classes and so did many colleagues.

Jim's renown as an educator was not only for his lectures, but also for his writings. Crow's *Genetics Notes: An Introduction to Genetics* (Crow 1983), written to help students follow his rapid-fire lectures, was a model of clarity. It quickly became famous and was used by genetics teachers worldwide. There were eight editions in this country (1950, 1951, 1955, 1960, 1963, 1966, 1976, and 1983) and translations into Japanese, Korean, Portuguese, Dutch, and Serbo-Croatian. The practice problems in Crow's *Notes* were challenging, but, with reasonable effort, almost every student could solve them. The problems were so aptly chosen and so well designed that students could hardly fail to understand the principles of genetics after they worked out the solutions. Many of the problems represented the latest work in the field. For example, in the 1966 edition, soon after the Genetic Code was finalized, there is a problem based on George Streisinger's frameshift mutations in the lysozyme gene of phage T4. This problem, which challenged both students and teaching assistants, appeared in the same year as the Streisinger article itself. Although the *Notes* were written as a supplement to the textbook, many students successfully used them in place of the textbook. Jim carefully updated the content until, finally, the field of genetics grew so large that no one-semester course could encompass the whole field. The field simply outgrew Crow's *Notes*.

Two figures in Crow's *Notes* deserve mention because they illustrate Jim's inventiveness and clarity. One shows the Genetic Code. Anyone who has taught genetics knows that students have a hard time learning to use the standard Code table, in which the first base in a codon is shown in the vertical column on the left, the second base is in the horizontal row across the top, and the third base is in the vertical column on the right. That is how the Code first appeared in Crow's *Notes*. But beginning with the 1976 edition, the Code was depicted in *two* forms: the conventional two-dimensional table and as a cube. The cubic version is instantly understandable. Jim claimed that he did not invent this ingenious format, although he could not remember the source—and no one ever came along to claim priority.

The other famous figure in Crow's *Notes* came from an article that Jim published in *The Journal of the American Statistical Association* in 1945 (Crow 1945), when he was at Dartmouth. Teaching a statistics course, he realized that the tables showing the probabilities of the chi-square and Student's *t*-distributions were both cumbersome and limited to probabilities of 0.05 and 0.01. It would be convenient, he thought, if the probabilities for various degrees of freedom could be read from a simple, one-page graph with a broader range of probability choices. Jim discovered a transformation that linearized the graph of chi-square vs. probability (and similarly for *t*) and produced a graph that instantly became the most requested of his many publications.

Thanks to Jim's extensive reading and his friendship with geneticists in virtually every branch, his lectures in general genetics were remarkably up to date. Here is one story that Jim liked to tell. The last codon to be decoded was UGA. In the 1966 edition of Crow's *Notes*, this codon was shown as "?," but in his lectures, Jim was able to reveal the not-yet-published meaning. The way he found out was that, one day in 1966, Jim was returning to Madison when a storm trapped him at O'Hare Airport. Among the other trapped Madison-bound travelers was UW colleague, Har Gobind Khorana (who later received a Nobel Prize for his research on the Code). Jim suggested to Gobind that they rent a car and drive back to Madison. On the way, Gobind told Jim the latest news—that UGA, the 64th codon, meant *stop*. So Jim now could reveal the meanings of all 64 codons to his general genetics students—hot news from the frontiers of genetics.

Jim's lectures tended to be a combination of often difficult, complex material and historical anecdotes and personal stories, told with wit and charm. He could make you think that something subtle or opaque was very easy. Often using the phrase "this is intuitively obvious," he would take a complex equation in population genetics and deftly reduce it to a few simple symbols that beautifully expressed some important concept. He might even tell you, as only a musician would, that "the equation sings." Sometimes, when studying for an exam, students might realize that something "transparently clear" to James F. Crow was not necessarily so clear to them, but this would stimulate them to figure it out for themselves. Anyhow, whether students "got it" or not, they knew that when they listened to Jim they were being treated to a virtuoso performance.

Jim had an extraordinary memory and a knack for weaving a charming story out of almost any experience. This was one of the reasons that everyone loved to hear him lecture. For instance, when describing his work with Motoo Kimura, Jim liked to add that Kimura used his royalties from their classic textbook *An Introduction to Population Genetics Theory* (Crow and Kimura 1970) to build a greenhouse in which he bred orchids. Kimura named one of his orchids the "James Crow." Happily, the James Crow won a prize, a botanical recognition that Jim valued as highly as an honorary degree (Figure 2). Another story that Jim liked to tell was this "Clash of the Titans" incident that he witnessed at a lunch with Joshua Lederberg and William Hayes. Lederberg asserted that *E. coli* crosses involved whole-chromosome interactions comparable to meiosis. Hayes argued, on the basis of his own experiments (Hayes 1953), that there was only partial transfer of a donor genome into a recipient cell and subsequent interaction between the recipient's whole chromosome and the donor fragment. Lederberg was such a crushing debater that Jim was persuaded that Josh had won this argument; later it became clear that Hayes was right.

Often students could remember Jim's jokes years after taking his course, and colleagues could recognize jokes that recurred. In one, Jim liked to point out that the human body contains numerous examples of *unintelligent* design produced

Figure 2 Prize-winning orchid bred by Motoo Kimura and named in honor of James Crow. The photo shows a tile painted by Kimura and given to Crow as a gift.

by evolutionary tinkering. He cited the example of the poor arrangement of trachea and esophagus, which tends to cause choking, and always ended his list with, “If you’re a male of my age, you’re very, very conscious of another thing, and that’s the location of the prostate gland. It couldn’t be in a worse place.” He repeated that lament for at least 35 years.

Jim was exceedingly generous in offering advice, constructive criticism, and support to his colleagues. For instance, Millard was a relatively young faculty member when asked to write a review of bacterial genetics for *Annual Review of Genetics*, a surprising invitation since Millard did no research on bacterial genetics and was scarcely known in the field. It was Jim who had engineered the invitation, knowing that Millard was up to date because he taught a course on microbial genetics. In the review, Millard explored Jacob and Wollman’s claim of high negative interference in crosses on *E. coli*. The evidence came from a seven-factor cross in which the only offspring examined were those that had experienced an even number of crossovers. After writing the large set of simultaneous equations to solve for the recombination distances, Millard was stuck and, after a couple of weeks of futile computation, went to Jim for advice. Jim said he would try to solve the problem over the weekend. On Monday, Jim delivered a bundle of paper covered with computations; it took him all weekend, but he had a “magical” breakthrough and found a maximum-likelihood solution. Millard, exceedingly grateful, asked Jim to be a co-author on the review. No, said Jim, he had fun doing the problem and would happily settle for mention in the acknowledgments. Many of Jim’s colleagues tell similar stories of receiving extensive and valuable help offered out of friendship and wide-ranging scientific curiosity. Oliver Smithies (Smithies 1995) recalls that, when he discovered evidence of an abnormal haptoglobin much larger than wild-type haptoglobin, he asked Jim Crow, “Is it possi-

ble for two allelic genes on homologous chromosomes to join together and give a double-sized gene? His response was to introduce me to the Bar locus in *Drosophila* with its long and fascinating history of homologous and nonhomologous recombination and gene duplication. This introduction served me well.” Following that hint, Smithies worked out the mysteries of haptoglobin gene structure and demonstrated that those outsized molecules were produced by unequal crossing over.

Music was so much a part of Jim’s life that no description would be complete without mention of his devotion to his viola and to his many friends in the music world. He started on violin when around eight years old and later switched to viola because, as he said, there is always a need for a violist. Jim continued to play all his life and, even at his retirement community, joined with musical friends to give regular recitals for the other residents. Whenever there was a large gathering to celebrate one of Jim’s landmark birthdays or one of his many honors, there were almost as many musicians present as scientists. Sally Chisholm, violist for the Pro Arte Quartet—one of Jim’s many philanthropic causes—says that for the past decade the Pro Arte and Jim got together every New Year’s Eve to play the Mozart G minor viola quintet. At midnight, as they opened the champagne, Jim proposed the toast—more peace in the world and another year of life for him! One of Jim’s favorite anecdotes linked science and music. He recounted “one of the diabolically cleverest jokes that anyone ever perpetrated,” played on him as a student in Texas. He had left his viola in the lab one day so that he could grab it quickly on his way to play in the orchestra for a musical comedy. One of his lab mates took the opportunity to pour thousands of anesthetized fruit flies into the viola, and they slept blissfully until the performance began. As Jim began to play, the flies slowly awakened and began to emerge from the f-holes and buzz about. Jim never left his viola in the lab again!

In 1986, to honor Jim’s 70th birthday year and his retirement, an International Genetics Symposium was presented in Madison by his students, postdocs, and colleagues, with two days of talks, by Lederberg, Morton, Kimura, Sandler, Baker, Mukai, and many others, on *Drosophila* genetics, including genetic loads, mutation rates, SD, transposable elements, theoretical population genetics, and other topics reflecting the great breadth of Jim’s interests and the research he directed. The Symposium concluded with a festive banquet featuring chamber music by Jim and his musician friends. Each of Jim’s milestone birthdays was cause for celebration, and notably, in January 2006, Jim presented a short recital to students and colleagues gathered in the genetics auditorium for the opening of the colloquium series, saying: “I have all the worldly goods I’d ever need, so I thought I would give everyone a present instead, a gift of music. Unfortunately it’s not returnable.”

During the quarter century after Jim retired, he continued to visit his office almost every day. He edited the *Perspectives* column of this journal for more than 20 years, along with Bill Dove. Of 298 pieces to date, Jim wrote 45—far more than any other contributor. He read as voraciously as ever and participated in the weekly Zoology and Evolution Reading

Group, in which we often read books suggested by Jim himself. He would enrich the discussion with personal anecdotes about people whose work was described in the book we were reading or by explaining a mathematical subtlety. Jim also faithfully attended the weekly Genetics Colloquium and regularly asked an incisive question or made a comment—shedding light on important points that the speaker had not made clear, or connecting the topic to some earlier discovery—that helped to provide “big picture” context. Most days, he typed away at the keyboard on his computer, exchanging ideas with colleagues at other institutions or writing one of the many articles published during those 25 years. Jim’s interest in the later years of his life often turned to historical issues in genetics and to the geneticists he knew and admired. His writings on these were not limited to *Perspectives*; he regularly wrote reviews, retrospectives, and biographical pieces for other publications as well. He was much in demand as a lecturer who could offer panoramic views of genetic issues from first formulation to the present day. During the past decade, he spoke and wrote on, among other things, paternal age effects, heterosis, additive genetic variance, opportunity for selection, and maintenance of evolvability—always finding new and interesting ways to look at problems that have been with us for years.

Jim’s memory and zest for life remained intact to the end. His final publication (Crow 2012) was written in his final weeks, when he was short of breath because of congestive heart failure. In telephone conversation with Bret Payseur, who was editor for the paper, Jim discussed the manuscript with his usual clarity and verve and only at the end of the discussion mentioned that he scarcely had enough breath to walk across his room. “But,” he said, “don’t worry about me. I’m fine.” And fine he was. He leaves behind a host of friends and admirers who will remember him—to borrow words from Kimura’s orchid plaque—as a “perfect man.”

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