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Envisioning a Woman Scientist

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Abstract

I entered science at a particularly lucky time. By the mid-1960s, women were being encouraged to pursue serious scientific careers. During the 60-year span of my career, women have become equal partners with men in scientific research, particularly in the biological sciences. There also has been abundant funding for research, which allowed me to succeed in a "soft-money" position at Smith-Kettlewell Eye Research Institute, a place that was especially supportive for a woman scientist with children. In this article, I describe the findings that I think represent the most interesting and enduring scientific work from my career.

INTRODUCTION

In 1963, when I entered graduate school, the University of California, Berkeley Psychology Department had no women on its faculty. Historically, two women, Olga Bridgman and Jean MacFarlane, had been part of the department, and Catherine Landreth was in the process of transferring from the Department of Home Economics to Psychology, where she remained until 1964. However, no *new* women faculty were added to the department in the 47 years between 1924 and 1971 (Weinstein et al. 2021). The Psychology Department was not alone in the dearth of women on its faculty. The percentage of women on the Berkeley faculty as a whole was about 4% in the 1960s. In 1925, Florence Sabin became the first woman elected to the National Academy of Sciences (NAS); 64 years later, women constituted only 3% of NAS. Undeniably, it was a discouraging picture for beginning women graduate students.

Fortunately for me, I entered science at the onset of the second wave of twentieth-century feminism. The development of reliable contraception meant that women had the freedom to decide if and when they had children, and so could pursue demanding careers. Still, coming from a blue-collar home, I had no strong aspirations for a career, certainly not for one in science. Neither of my parents had attended college, but I knew that I wanted to go to college. My father had gently explained that there was not enough money in our family to send a girl to college; the money was reserved for my two brothers' education, as they would have to support a family. Then he added that if I wanted a college education, I had to win a scholarship. Stimulated by this challenge, I became a ferocious "grind" in high school, and when Vassar College offered me a scholarship, I took it.

VASSAR COLLEGE

My journey from El Cerrito, a small town just north of Berkeley, to Poughkeepsie, NY, where Vassar is located, was the longest of my young life. I had never before left California, never before taken a flight, a train trip, or a taxi ride, and in one day, all those things changed. Of course, the biggest change was profoundly cultural. Vassar was then one of the Seven Sisters, the colleges for women that paralleled the all-male Ivy League schools. It was an outstanding liberal arts college committed to educating women in all aspects of human knowledge. There were required survey courses in the fine arts, literature, history, philosophy, and science—a dazzling intellectual experience for someone as naïve as I was then. Vassar taught me to think and write clearly, although my scientific training there was somewhat meager due to my own preferences for courses in philosophy and history instead of physics and mathematics.

On entering Vassar, I had a vague plan that I would major in history and obtain a credential for teaching in high school. However, when I took my first course in psychology, I was hooked. A dynamic young teacher, Margery Bodansky Franklin, made psychology, particularly her specialty, psycholinguistics, seem an exciting new subject. More importantly, I discovered that I enjoyed designing and implementing experiments. In the 1950s, laboratory courses in science consisted chiefly of replicating ancient experimental findings; it was a time of "inclined planes" and "pithed frogs," nothing to tax a student's imagination. Psychology, in contrast, required students to design original experiments, or experiments that differed at least minimally from well-known results, since few experiments required complicated and costly equipment. No experiment I completed as an undergraduate deserves mention here, but my delight in experimental design and execution remained as the motivating force of my career.

GRADUATE SCHOOL AT UC BERKELEY

With the encouragement of my mentor, Dr. Franklin, I decided to go to graduate school, applying *only* to UC Berkeley. What hubris! My only excuse for my unwarranted confidence was that I

wanted to go home. Fortunately, I was admitted to the Ph.D. program in psychology at Berkeley, where I was planning to study developmental psycholinguistics. Although two outstanding psycholinguists, Dan Slobin and Susan Ervin-Tripp, would soon join the psychology faculty, there were no psycholinguists on the faculty when I arrived in Berkeley. At the urging of my then-boyfriend, I transferred my interests to Tom Cornsweet's vision laboratory. Cornsweet wanted to study the all-cone eyes of ground squirrels, so he assigned me the task of measuring their color discrimination using operant conditioning. I had never before worked with animals or designed a circuit, much less built one, but soon I was feeding ground squirrels and soldering banks of relays into some sequence that would reward the beast for choosing the correct side in a 2AFC task with luminance randomized to guarantee that the choice was based on color differences, not brightness. To my complete surprise, the system actually worked after many months of effort. As I recall, I managed to obtain one psychometric function from one particularly thirsty creature before Cornsweet decided that he was tired of teaching and left Berkeley for industry. All that "wasted" effort taught me many things about vision and psychophysics; in particular, I learned that I could build the equipment needed to answer an experimental question. Thankfully, relays were about to give way to computers.

Two noteworthy things occurred during my first two years of graduate school. First and most important, I met and married my husband, Chris McKee, then a physics graduate student. Chris has had a brilliant career as an astrophysicist, completing a long tenure as a UC professor of physics and astronomy; we have three children, four grandchildren, and 57 years of nurturing companionship. The second thing was that I met and became friends with Gerald Westheimer. I was auditing an evening course that Gerald was teaching on optics, eye movements, and psychophysics. He said something intriguing about the uncertainty principle in the context of human cones, and I came to talk to him about it after class. After a pleasant conversation, I invited him to come for dinner and to talk with my husband, who was getting a degree in physics. Shortly after that, I began a reading course with Gerald—a course that cemented our friendship.

With Cornsweet's departure, Gerald invited me to become his graduate student. Gerald had recently published an important paper on an effect that came to be known as the Westheimer paradigm (Westheimer 1967). He had measured the increment threshold for a tiny spot positioned in the center of a small circular luminous patch. As the diameter of the circular patch was increased, the threshold rose and then fell at greater diameters. The psychophysical data bore a startling resemblance to the center-surround organization of retinal ganglion cells—an inhibitory surround that reduced the excitation produced by the smaller-diameter central patch. Gerald then showed that the sensitizing effect of the "surround" occurred only within the cone system; there was no rod–cone interaction (Westheimer 1970). He suggested that my dissertation research should explore whether this sensitizing surround effect occurred within or between color mechanisms, using Stiles's psychophysical technique for isolating the middle- and long-wavelength mechanisms (Stiles 1949). I had expected to find psychophysical evidence of color opponency, consistent with DeValois's studies on macaque lateral geniculate neurons (DeValois et al. 1966). Instead, my results showed that the sensitizing action of the surround on the center occurred within cone mechanisms, not between them (McKee & Westheimer 1970). I was very disappointed with this outcome, because like most psychophysicists, I wanted to show a link between my behavioral data and physiological results, however logically tenuous that link might be (Teller 1984).

THE POLAROID VISION LABORATORY

Chris and I suffered from the "two-body" problem common to most academic couples—finding neighboring positions that would allow each of us to pursue our own careers while preserving an intact family life. Perhaps due to my upbringing, we had agreed that he would seek the best possible

job, and I would try to find a teaching slot at some nearby small college. This decision was less of a sacrifice on my part than it sounds. I didn't think that I was good at research, and I had enjoyed the limited amount of teaching that I had done previously. Unfortunately, our arrangement fell apart when Chris became an assistant professor at Harvard. The 20-plus resumés I sent to colleges in the Boston area received no positive replies—I was out of work. Once again, Gerald came to my rescue. He wrote to John McCann, who was in charge of the vision research laboratory at Polaroid, and suggested that, given my knowledge of color vision, I might be useful as a part-time employee in his research program. John interviewed me, introduced me to Edwin Land, and hired me half-time.

One major function of the vision laboratory was to test Edwin Land's theory of color vision (the Retinex theory). Land had created some amazing demonstrations of color constancy that had thrilled large audiences for several years. His explanation for these effects was a kind of normalization within each color pathway that partially corrected for the illuminant via extensive interactions across the whole visual field, weighted inversely by distance. John McCann had fleshed out the details of Land's model and had constructed a computer program based on its operations—one of the earliest computational models of human visual processing. To see whether the program imitated actual human color vision, John needed well-controlled measurements of what observers perceived. We constructed a test pattern consisting of many differently colored rectangular pieces of matte paper pasted together on a flat surface (the "Mondrian") and viewed under parametrically varied illuminants. Each rectangle viewed under each test illuminant was matched to one of the color swatches in the Munsell book of colors, viewed under a standard illuminant. By the end of the experiments, I had memorized the entire Munsell book.

The Retinex model performed well, replicating the human choices (McCann et al. 1976). Even though the model's operations bore little resemblance to physiological measurements of primate color processing, it was exciting to test its capabilities. John McCann was a great boss, and I enjoyed my three years at Polaroid.

HYPERACUITY

Alerted by Gerald that there was an opening in the Physics Department, Chris applied for the position and was appointed an assistant professor at UC Berkeley in 1974; I became Gerald's research assistant the same year. Gerald had just obtained a new PDP-11 computer that he loved programming. The computer occupied about three closets' worth of space and had considerably less computational power than the original iPhone, but it removed the need for an additional "experimenter" to take data and manipulate equipment while the "observer" waited patiently for the next stimulus presentation; this meant that you could take measurements on yourself without additional help. Being a certified "data freak," I often endured as many as 2,000 trials per day in pursuit of an answer. I must admit to one bit of serious craziness—I really enjoy taking measurements on myself.

Our best-known experiments together were on the positional acuities that Gerald labeled "hyperacuities." He used this term to distinguish them from resolution acuity. The ability to identify the location of a feature with respect to another feature is substantially better than resolution acuity—typically amounting to a precision of 10 arcsec or less. **Figure 1** shows examples of the various hyperacuities. On each trial, the observer makes a binary judgment about relative location: Vernier (upper line to the left or right), Orientation (tilted left or right), Bisection (center line closer to the left or the right outer lines), Motion (moved left or right), and Stereoacuity (upper line in front of or behind lower line).

Many measurements of hyperacuity had been made in the late nineteenth and early twentieth centuries, but the topic had been largely neglected for several decades. *Vision and Visual Perception*,

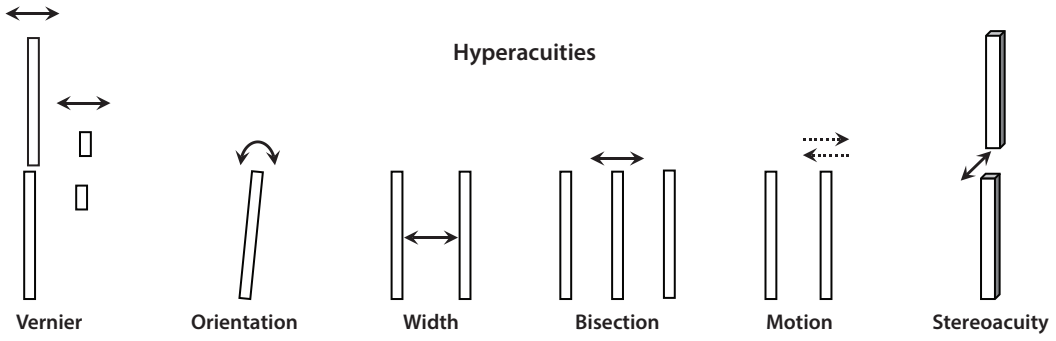

Figure 1

Line targets used to measure hyperacuity thresholds.

the 1965 compendium of all visual psychophysics, devotes a scant two paragraphs to spatial localization, while including five full chapters on color vision (Graham et al. 1965). Thus, Gerald and I were free to expand on old studies, as well as to compile some completely novel results. We found that Vernier acuity was unaffected by moving the target laterally at speeds ranging up to 2 deg/sec; stereoacuity was similarly unaffected by the same range of lateral speeds (Westheimer & McKee 1975, 1978). We explored the spatial constraints (line length, separation, etc.) on many of the configurations shown in **Figure 1** and confirmed Ludvigh's (1953) observation that Vernier acuity for bright points was as precise as for long lines, provided that the points were optimally separated (Westheimer & McKee 1977b). This result proved that the traditional explanation for the precision of Vernier acuity—averaging along the length of the target lines to improve the estimate of line location—was incorrect. We also replicated and extended Berry's (1948) observation that stereoacuity was not limited by the monocular position acuity for the half-images (Westheimer & McKee 1979), a result that argues that stereoacuity depends on an entirely different visual mechanism than Vernier or bisection acuities.

So what made hyperacuity interesting? Partly, it was that Gerald was a brilliant salesman; he used his Proctor Lecture at the Association for Research in Vision and Ophthalmology in 1979 to highlight the differences between resolution and localization acuities (Westheimer 1979). More compelling still were the actual threshold values—hyperacuity thresholds were smaller than the diameter of a single foveal cone, which seemed superficially inexplicable. In fact, there is nothing mysterious about this outcome. Although thresholds are smaller than a cone, the light distribution produced by a single point extends over many cones. Astronomers can localize the position of a star with a precision that is far greater than the resolving power of a telescope; they use "centroiding." The precision in determining the mean position of a star from its light distribution depends on the amount of measurable light coming from the star; if the star is very bright, the whole light distribution including the tails can be used to determine the centroid. In contrast, if the image is blurred by poor resolution, the number of quanta that define the tails of the distribution may fall below the signal/noise limits of astronomical instrumentation, making localization less reliable. Thus, resolution can influence localization, but if there is enough light, stars can be localized to an arbitrary precision.

These considerations show that the information about location is present in the retinal image, but not how the visual system acquires it. Why, after all, are these hyperacuity judgments always made in relation to another nearby feature? Does oculomotor jitter make it impossible for the visual system to assign a precise location to an isolated feature on the retinal mosaic? There is evidence that the human visual system also uses "centroiding" to localize features (Westheimer

& McKee 1977a, 1978; Watt et al. 1983), but what sets limits on the precision of localizing one centroid with respect to another? The answer was about to emerge.

While Gerald and I were busy making hyperacuity measurements with lines and dots, most of the psychophysical community was measuring contrast sensitivity and adaptation using sinusoidal gratings of various spatial and temporal frequencies, orientations, directions, and depths [summarized cohesively in Graham's (1989) book, *Visual Pattern Analyzers*]. The number of papers appearing in the 1960s, 1970s, and 1980s employing gratings is simply astonishing. The objective of all these measurements was to identify the spatial and temporal mechanisms that initially analyzed the visual image into components and to obtain psychophysical results that could be related to emerging data on neural responses in primary visual cortex.

In the mid-1980s, several groups (Klein & Levi 1985, Nakayama & Silverman 1985, Wilson 1986) had the same insight: Hyperacuity thresholds were determined by the contrast sensitivity of the same spatial mechanisms that had been the subject of so many studies. Small shifts in position would produce something akin to a change in contrast, and if the change reliably exceeded the contrast threshold, then it could be detected (Shapley & Victor 1986). Of course, some subsequent stage has to read out the pattern of activity to determine whether a contrast increment or a positional shift had produced the change, but the precision of hyperacuity (the 10 arcsec) was explained by this approach. Creating a link between spatial localization and contrast sensitivity was a kind of scientific triumph, but a short-lived one. By the late 1980s, psychophysicists were becoming bored with contrast sensitivity and sinusoidal gratings, and we were certainly boring. What became interesting was not what these early visual mechanisms could explain, but rather those aspects of image processing that weren't trivially explained by these mechanisms—visual search, attention, contour formation, face identification, natural image statistics—all topics that would intrigue psychophysicists in the coming decades.

SMITH-KETTLEWELL

By 1980, I was approaching age 40 and was still working as a superannuated postdoc in Gerald's laboratory. It was clear that our fruitful collaboration could not continue in perpetuity. What could I do? My husband had tenure at Berkeley, and we had three children and an enduringly happy marriage. There were no academic jobs to be had in the Bay Area. So I began taking night courses in accounting, thinking that my love of numbers might be put to some profitable use. However, I had heard of the Smith-Kettlewell Eye Research Institute, a small nonprofit dedicated to vision studies, and I knew one Smith-Kettlewell principal investigator, Ken Nakayama, who had been a postdoc in Berkeley when I was a graduate student. I called Ken and asked whether I could join the scientific staff of Smith-Kettlewell. He was not very encouraging, since the Institute already had two excellent psychophysicists (himself and Christopher Tyler) on its staff—why did it need a third? Nevertheless, Ken managed to persuade the director, Arthur Jampolsky, that I might be useful as a half-time administrator, and that I could devote the other half of my time to science, if I could obtain funding.

My decision to join Smith-Kettlewell was daunting. The Institute expected you to raise your own salary as well as the salary of your assistants by obtaining federal grants. Living on "soft money" is a bit like coming up for tenure every three years forever. Sensing my fears, Ken was very supportive and helped me adjust to being a principal investigator (PI, which he translated as "pretty important" person). To my amazement, I was successful in obtaining two grants, one from the National Eye Institute (NEI) and one from the US Air Force, which allowed me to give up the administrative portion of my position and to hire some part-time assistants (Leslie Welch and Doug Taylor). Of course, once funded, you have to complete the research.

In some respects, Smith-Kettlewell is an ideal place for scientists raising children, i.e., women. Your only job is to get funded, so your time is completely flexible. You can program in the middle of the night, collect data on Sunday afternoons, and write papers after dinner—just like women scientists at academic institutions. But you are not required to teach, so you have more time for research (and your children). However, because you have no graduate students, you have less research help, fewer people to design and complete experiments, and fewer people to author papers. In my case, two of my children worked as my lab assistants when they were home from college for the summer, which is one way to get decent help. On the whole, it is the environment of friendship and mutual support that distinguishes Smith-Kettlewell from most other institutions, and this environment is especially important for women scientists at the beginning of their careers.

In lieu of graduate students or postdocs, I began collaborating with scientists from other institutions, including Dennis Levi, Eileen Kowler, Michael Morgan, Davida Teller, Stan Klein, Richard Harrad, Gordon Legge, and Laurie Wilcox. Particularly important to my subsequent work on stereopsis was my long-distance collaboration with Graeme Mitchison, whose home institution was Cambridge University. Graeme was interested in stereo matching because of its status as an important problem in computational vision (Marr 1982). During one of his visits to the Bay Area, Graeme, using my stereoscope, began programming repetitive patterns of points to see how they were matched stereoscopically, because stereo matching for repetitive patterns is inherently ambiguous. After controlling for fixation in one plane, he briefly presented a row of regularly spaced points and asked observers to judge whether a variable disparity test point appeared in front of or behind the row. He then shifted the regularly spaced row of points by one period and discovered that the whole row of points appeared in the depth plane defined by the disparity of the edge points, not in the fixation plane. In contrast, if the eyes remained fixated on a position in front of (or behind) a row presented for an extended duration, the initial edge-based match was replaced by a match in the fixation plane at retinal correspondence—a shift in depth that usually took several seconds (McKee & Mitchison 1988). Edge-based matching was found for rows, with interpoint spacing of 10 arcmin, for widths ranging up to 5–6 deg. How did the edge disparity, 2–3 deg away, affect the match in the center of the row, especially given that the stereo system had an alternative match at retinal correspondence?

Based on our results, Cumming & Parker (2000) were intrigued by the effect of an aperture on the responses of disparity-sensitive neurons in primary visual cortex (area V1). They presented a sinusoidal grating within a small circular aperture, which stabilized the depth percept unambiguously at the disparity of the aperture for both human and macaque observers. They then measured the disparity response of a neuron sensitive to a region within the aperture as they varied the disparity of the aperture. Although the apparent depth of the grating segment changed with shifts in the aperture, the neuron's response was unaffected by the aperture's disparity, showing that perceived depth is not determined by V1 disparity-sensitive neurons. However, Prince et al. (2000) showed that some V1 neurons were sensitive enough to small changes in disparity to underlie the precision of stereoacuity judgments in macaques and presumably their human relatives. If subsequent stages of disparity processing can access this precise information, stereoacuity is undoubtedly limited by the sensitivity of these V1 neurons.

How does the disparity of the aperture (envelope) affect psychophysically measured stereoacuity thresholds for an extended grating segment? It is well known that, as a stereo target composed of lines (see the stereoacuity target in **Figure 1**) is moved away from the fixation plane, stereoacuity thresholds rise exponentially (Blakemore 1970, Ogle 1953). McKee et al. (2005) measured stereoacuity for a 6-deg-wide, 3 cyl/deg grating in a rectangular envelope as a function of the envelope's standing disparity. The phase disparity of the grating was incrementally changed from trial to trial, and the subject judged whether the grating appeared in front of or behind a

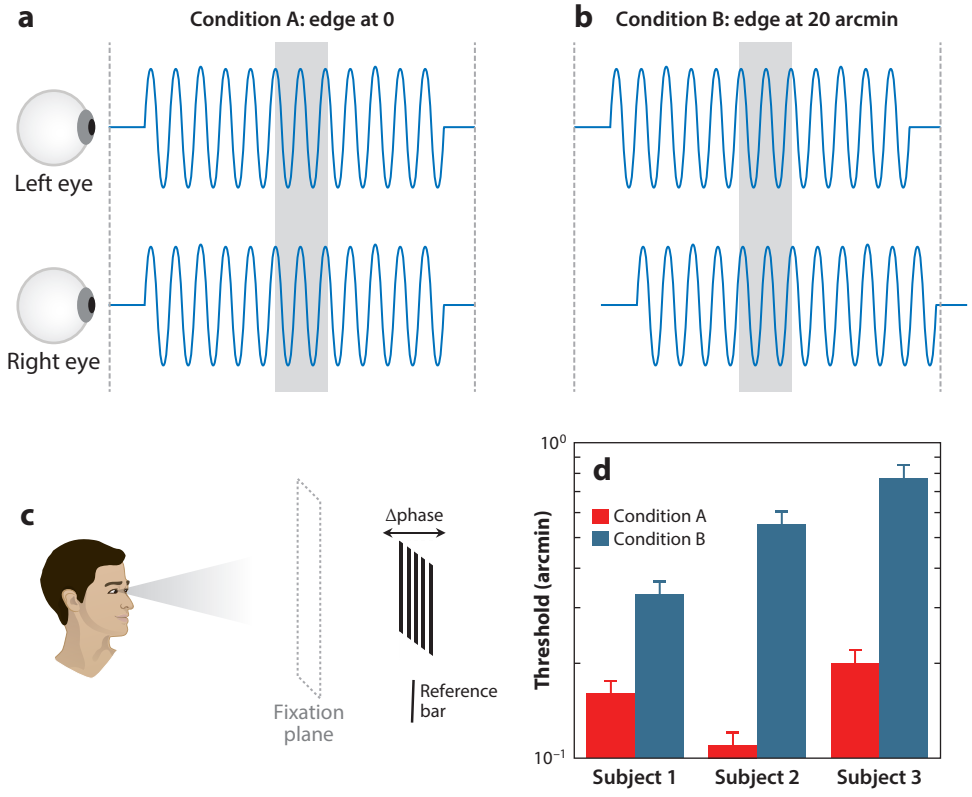

Figure 2

(*a*) Grating (3 cyl/deg) presented at retinal correspondence in the fixation plane (0 disparity). (*b*) Grating (3 cyl/deg) shifted by one full period, so that the envelope ("edge") is presented 20 arcmin behind the fixation plane. Note that the disparity of the central region outlined by the gray rectangles is the same for both conditions. (*c*) Diagram showing the display arrangements for the subject. The phase disparity of the grating is varied from trial to trial, and the subject judges whether it is in front of or behind the reference bar, which is presented in the plane of the envelope on every trial. (*d*) Thresholds from three subjects for conditions A and B.

fixed reference target located below the grating (see the diagram in **Figure 2*c***). We found that stereoacuity thresholds for extended gratings increased with increasing envelope disparity, just like line targets. When the envelope disparity was increased to one full period of the grating (20 arcmin), the central segment of the grating (e.g., the region within the gray rectangles in **Figure 2*a*,*b***) was identical to a grating presented in the fixation plane. But clearly, as the data in **Figure 2*d*** show, the thresholds for the shifted grating are dramatically higher than those in the fixation plane. Note that presenting the reference line in the fixation plane when the envelope is shifted by one full period does not improve thresholds for that condition.

Like the row of dots, if the eyes remain fixated on a point in front of the envelope-shifted grating (**Figure 2*b***), the grating will appear to shift in depth from the edge plane to the fixation plane after a few *seconds* (wallpaper illusion). McKee et al. (2007) demonstrated that the envelope mechanism adapts, thereby permitting the alternative match at retinal correspondence. Perhaps our most interesting result was that, once the envelope adapts so that the grating shifts to the depth of the fixation plane rather than appearing 20 arcmin behind the plane, stereoacuity for the grating improves fivefold without any change in the stimulus. We speculated that access to

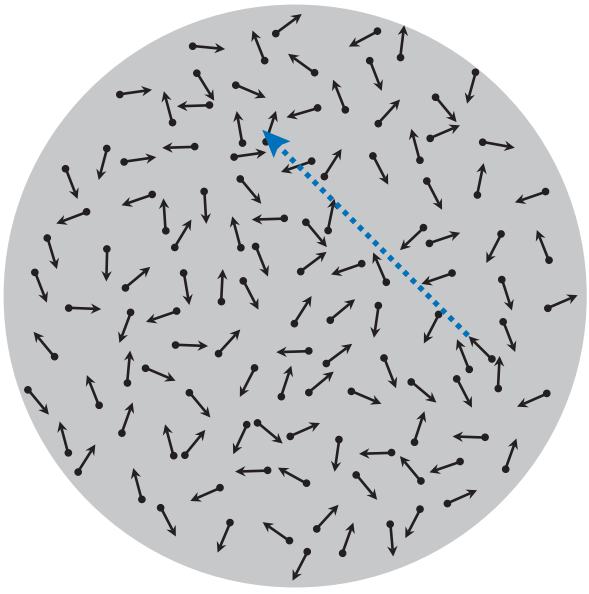

Figure 3

Trajectory presented within Brownian motion noise. The trajectory moves in the same direction on every frame, while noise dots move in randomly chosen directions. The location and the direction of the trajectory are randomized from trial to trial.

the most sensitive disparity detectors in V1 is gated by the extrastriate processes that determine perceived depth.

In 1989, I recruited my first postdoc, Scott Watamaniuk. For his dissertation in Bob Sekuler's laboratory, Scott had measured direction discrimination for stimuli composed of dots, in which on each frame, each dot moved one step in a direction chosen randomly from a specified range of directions (Watamaniuk et al. 1989). He brought this same paradigm to my laboratory but with an interesting variant. How detectable is a single dot that continues in the same direction on every frame when embedded in a noise background composed of dots moving in random directions on every frame (**Figure 3**)?

The trajectory dot appeared at a random location within a central square, 2 deg on a side, and moved in one of eight directions, chosen at random; within a single frame, the temporal and spatial characteristics of the trajectory dot were indistinguishable from the noise dots. I suggested that the trajectory was easily detected because it generated a strong response within a local motion detector, whereas the responses produced by the noise dots were incredibly weak. Scott is a very clever experimentalist, so he quickly designed an experiment to counter this suggestion. What happens to detectability if the motion trajectory follows a circular path? We found that a curved trajectory, which changed direction by 72 deg within 100 msec, was as easily detected as a straight trajectory (Watamaniuk et al. 1995). It is unlikely that a motion detector would be equally stimulated by these two paths. So what does account for the detectability of the trajectory?

Shortly after Scott left for a position at Wright State University, Preeti Verghese joined Smith-Kettlewell. She had been working on visual search with John Palmer and Misha Pavel (Palmer et al. 2000), and she immediately saw trajectory detection in motion noise as a type of search task. First, she performed some additional experiments to rule out the role of local motion detectors mediating trajectory detection (Verghese et al. 1999). Preeti then guessed that the enhanced activity

in a motion detector generated by the initial segment of the trajectory was acting as a cue to the projected pathway of the trajectory as a whole. It is well known that a cue signaling where a target will appear increases contrast sensitivity for that target (Carrasco 2006). When the target location is unknown, the cue, via selective attention, reduces the number of local detectors that are being monitored and thus effectively reduces uncertainty about target location.

As evidence supporting her idea, Preeti showed that the contrast threshold for an increment added to the trajectory dot for the last 70 msec of a 200 msec trajectory was far more detectable than an increment added to the first 70 msec. Moreover, the psychometric functions for the two conditions (increment-first and increment-last) were quite different. Under conditions of high uncertainty, the psychometric function is very steep—more like a step than a sigmoid. The function for the increment-first condition was very steep, whereas the function for the increment-last condition was shallower, indicating that the cue provided by the initial section of the trajectory was reducing uncertainty. The visual system was predicting the future direction of a moving feature in noisy conditions, a useful strategy for human survival (Verghese & McKee 2002).

AMBLYOPIA, INC.

Monocular amblyopia is a developmental abnormality that results in a loss of visual acuity in one eye with no detectable organic cause. It is typically associated with strabismus (crossed eyes) or anisometropia (a significant difference in the refractive errors of the two eyes) during early childhood. John Flynn, a well-regarded pediatric ophthalmologist, was frustrated that the treatment for amblyopia had not much changed in over 200 years; basically, the better eye was patched or penalized to force use of the amblyopic eye with the aim of strengthening its visual functions, particularly acuity. He thought that there might be many kinds of amblyopia and that treatment could be improved if it were tailored to the specific abnormalities.

John had been impressed by a paper by Levi & Klein (1982) showing that the relationship between grating acuity and Vernier acuity was different in anisometropic amblyopes than in strabismic amblyopes; in anisometropes, Vernier thresholds increased almost linearly with the losses in grating acuity, while in strabismics, Vernier thresholds were proportionately much higher than predicted from their grating acuity. John reasoned that if numerous psychophysical and oculomotor measurements were made on a large number of amblyopes, as well as individuals with the associated conditions of strabismus and anisometropia ("at-risk" subjects), distinct patterns of abnormalities might emerge, characterizing different types of amblyopia. In 1983, John began, using his own funds, to invite groups of ophthalmologists and psychophysicists to small meetings. The aim of these meetings was to design a clinical and experimental protocol for a large clinical study, involving many ophthalmological centers, and to write a proposal to obtain NEI support for this study. Unfortunately, the then-director of NEI, Dr. Carl Kupfer, was opposed to this type of clinical study, since multiple centers were costly and often failed to produce the promised results.

How I came to be the PI on the amblyopia grant remains somewhat mysterious even to me. Of all the people that John assembled in the hopes that they would be willing to participate in his proposed study, I knew the *least* about amblyopia and its associated conditions. Oddly, after a meeting with John Flynn's group in San Francisco, Dr. Kupfer challenged me at Smith-Kettlewell and Cliff Schor at UC Berkeley to run an NEI-funded pilot study showing that we could make psychophysical and oculomotor measurements on a large contingent of suitable subjects. Thanks to the extraordinary effort and organizational talent of Nance Wilson, we ran more than 180 subjects during this pilot phase of the project. Impressed by this outcome, Kupfer agreed to support a larger, full-fledged study of amblyopia, but again only at Smith-Kettlewell and Berkeley. With the advice of many others, notably Tony Movshon and Dennis Levi, Cliff and I designed the

experimental protocols. Again, Nance organized a procedure for recruiting subjects, set up appointments for clinical evaluations, found suitable research assistants, and arranged sessions for the experimental measurements.

At the end of three years, we had collected a vast array of clinical and experimental data on 427 amblyopic and at-risk subjects, plus 68 normal controls. Cliff and Nance managed to extract an interesting result from our data showing that oculomotor behavior patterns in adult strabismics predicted the age of onset of their strabismus (Schor et al. 1997). I, in contrast, had no idea how to assemble a coherent story from our massive database. I was particularly upset that our measurements of Vernier and grating acuity did not show the difference between strabismic and anisometropic amblyopes that Dennis Levi and Stan Klein had reported. It is a persistent conceit of psychophysicists that very careful, detailed measurements made on a small number of normal subjects can be taken as a description of sensory processing in the normal population as a whole. Whatever the truth of this idea for normal vision, it didn't seem to extend to our abnormal population.

Then NEI invited me to a conference on vision screening in preschool children and asked me to talk about our results (McKee 1998). We had paid little attention to our two measurements of binocularity, stereoacuity and a novel dichoptic motion task, so I decided to include the binocular results in my talk. If I scored the binocular measurements as simply pass or fail, subjects who failed one test tended to fail the other, while subjects who passed one also tended to pass the other. Predictably, most strabismic subjects failed both tests. The unexpected result was that many anisometropes, including some who were classified as amblyopic, passed both tests (Levi et al. 2011). Once the acuity in the weaker eye was worse than 20/100, no subject had any residual binocularity, but anisometropes with mild-to-moderate acuity loss were likely to pass both tests.

I wondered whether the difference between strabismics and anisometropes identified by Dennis and Stan depended on their binocularity. As I suspected, the Vernier acuity of our binocular anisometropes showed the same pattern of loss as the anisometropes in the Levi-Klein study, but the pattern in the non-binocular anisometropes resembled that of the strabismics. The reason why we were not replicating their results was because their small sample was based on mild-to-moderate amblyopes, while ours included many severe amblyopes, who all lacked binocular function. Birch & Swanson (2000) had described a related finding; anisometropic amblyopes with acuities better than 20/80 followed the Levi-Klein pattern, whereas severely amblyopic anisometropes (acuity worse than 20/100) resembled strabismics.

Tony Movshon began visiting the Bay Area regularly as he, Dennis, and I tried to impose some order on our psychophysical data. Tony was not convinced that there were any compelling differences among the different clinical groups (ultimately subdivided into 10 based on their clinical profiles) except that some groups suffered more severe visual losses than others, but he was willing to put that idea to the test. We decided to focus on five measurements from the weaker eye that were commonly used to study amblyopia: grating acuity, Vernier acuity, optotype acuity, edge contrast, and Pelli-Robson contrast. Factor analysis showed that these five could be represented by two factors: an acuity factor and a contrast factor. Obviously, there are high correlations among the three acuity measures and, similarly, a high correlation between the two contrast measures.

The value of the resulting paper depends heavily on the unusual statistical approach Tony used to identify real differences among different subgroups. In our data set, the distribution of acuities of the weaker eye was very skewed. Most of our abnormal subjects, whether classified as "at risk" or amblyopic, had acuities ranging between 20/20 and 20/60, but because we had such a large sample, the acuity of a few subjects reached 20/2000. Thus, traditional statistical analyses based on a normal distribution were invalid. Instead, Tony used permutation analysis, which makes no assumption about the underlying distribution, to determine whether observed differences were

statistically significant (often running calculations late into the night!). I began pestering Tony to look at how binocularity affected the data, and finally, to humor me, he looked at the binocular effects. To his surprise and mine, the statistical differences between binocular and non-binocular subjects was large and highly significant.

Eventually, Tony's hard work became a graph with one axis being the acuity factor and the other the contrast factor. Tony had calculated an acuity factor and a contrast factor for the weaker eye of every subject; he used the average factor values associated with each clinical group to show where the groups fell within this graph. Binocularity split this graph in half, with all types of strabismics on one side and the anisometropes on the other. One curious outcome was that the *pure* strabismic group had slightly better contrast sensitivity than the normal group (and much better than the *pure* anisometropes)—a result that could be explained by their loss of binocularly driven neurons and their increase in monocularly driven neurons.

Strabismus and anisometropia are not different diseases in the sense of measles and mumps, but these two abnormalities have quite different effects on visual functions. The blurred image arising from anisometropia degrades acuity and contrast sensitivity, while the loss of binocularity in strabismus is associated with unsteady fixation in the deviating eye. It may be that this unsteadiness explains why their Vernier and optotype acuities are worse than predicted from their grating acuity for a horizontal grating. This unsteadiness and the consequent corrective saccades may also explain why saccadic latency is so much longer in strabismics than in anisometropes (McKee et al. 2016).

McKee et al.'s (2003) paper has become the second-most-cited paper on amblyopia (Allon et al. 2023). I have the strong suspicion that it is often cited but seldom read. Nevertheless, it is gratifying that this paper has such a wide audience, because it was ultimately the result of three friends doggedly trying to bring order out of chaos.

SOME CONCLUDING THOUGHTS

In 2022, nearly 60 years after I began my career, it is hardly worth noting that a scientist is a *woman*. Nearly half of the newly elected members of the National Academy of Sciences (NAS) are women; the current NAS president is Marcia McNutt. The chair of the UC Berkeley Psychology Department, Serena Chen, is the fourth women to chair the department, and 48% of the department's faculty are women. Vision science has been particularly supportive of women; the first authors of 17 of the 35 articles in the 2021 volume of the *Annual Review of Vision Science* are women. The nineteenth century believed that society was "progressing" toward an improved and enlightened state, but the twentieth century demolished that belief as our species used its phenomenal intellectual ability to become more adept at killing each other on an unprecedented scale. Nevertheless, one aspect of human endeavor does progress—science. Science does not give up its hard-won understanding of the natural world, but builds success on previous successes. Women may face serious backlash in political domains, but not in science. We are here to stay. All you have to do to succeed in science is be smart, creative, hardworking, and ambitious. Fortunately, those attributes don't seem to be uniquely located on the Y chromosome.

My own personal success has depended on many people: my supportive husband, Chris, and children (Arthur, Chris and Maria); my mentor, Gerald Westheimer; my colleagues at Smith-Kettlewell, particularly Preeti Verghese, as well as my postdocs (Scott, Preeti, Harvey Smallman, Julie Harris, Anna Ma-Wyatt, Sam Bowne, Mary Bravo, Andrew Glennerster, Yury Petrov, Mark Pettet, and Scott Steinman); and my student, Leslie Welch. In this article, I have highlighted the scientific discoveries that seem to me to be the most interesting and enduring contributions from my laboratory. Obviously, none of these results are based on my work alone. Indeed, it is hard for me to imagine how I could have continued in science for the last 20 years without the intelligence and creativity that Preeti has brought to our varied collaborations.

Finally, I must acknowledge the immense contribution of "Group," a support group that I joined in 1980. This group, which never included a therapist, was focused on problem-solving rather than "consciousness-raising." Initially, the group included men as well as women, but by the time that I joined, it was composed only of women. When I was trying to decide whether to leave science or take a chance on surviving in a soft money position, it was "Group" that advised me to join Smith-Kettlewell ("you could always become an accountant next year"). They provided advice on writing grants, running a laboratory, giving talks, and managing postdocs.

In the early 1990s, "Group" coalesced into the eight women who have been meeting together for the last 30 years. What an amazing group of women! Four of the eight of us are (or were) members of the NAS: Christine Guthrie, Carol Gross, Judith Klinman, and Mimi Koehl. Another member of the group, Beth Burnside, served as Dean of Life Sciences, and then Vice Chancellor for Research, at UC Berkeley. Ellen Daniell, the member who authored the book *Every Other Thursday* (Daniell 2006), which describes our group, was the first woman faculty member hired by the Molecular Biology Department; she left academia for a job in the biotech industry. The eighth member of our group is our beloved Helen Wittmer, age 93, a former administrator of the UC Berkeley Molecular Biology Department, whose wisdom, compassion, and humor continue to guide us all. Recently, we lost the founding member of our group, Christine Guthrie, who died in July. I dedicate this article to her memory and to the courage and wise counsel she gave me during my 42 years as part of her group.

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