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SYNCHROTRON RADIATION AND DETECTORS: SYNERGISTS IN A DANCE

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Growth in the use of synchrotron radiation for crystallography has been driven as much by advances in detectors as availability of storage ring sources. A brief, personal historical survey of the development of TV and CCD detectors is provided. New detector technologies have deep roots and often gain wide acceptance years after the fundamental problems have been resolved. In the case of CCD detectors, the ground work goes back about thirty years, with the last fundamental problems having been solved by the early 1990's. The article concludes with a brief description of some promising new detector technologies now in development.

1. INTRODUCTION

Recent growth in the use of synchrotron radiation in many areas of science has been driven as much by advances in detectors as availability of storage ring sources. For example, in the U.S. between 1985 and 1995 there was an enormous change in the fraction of macromolecular structures solved using synchrotron radiation, even though there was only modest change in the number of synchrotron beam lines. The big change over this time span was that newer detectors shrank the time required to obtain crystallographic data sets from days or weeks to mere hours. Synchrotron radiation and better detectors together catalyzed advances that are now enabling new types of systematic studies that, just a few years ago, would have been beyond consideration.

This report is a personal history of the development of CCD detectors, especially as applied to macromolecular crystallography. In the spirit of this session, the emphasis is on the word personal. It would be impossible in the constraints of a short report to give a full accounting of the many developments by others that led to the present CCD detector revolution going on at storage rings around the world, much less to give a full history of all synchrotron detector developments. So please understand that this is only part of the story.

Although CCD detectors seem new to most users, from a detector designers point of view the last major problem was solved almost a decade ago, the culmination of two decades of earlier work. My point, of course, is that new technologies usually have deep roots that are not at all obvious. My purpose here is to trace those roots as I recall them.

2. TV DETECTOR DEVELOPMENT AT PRINCETON UNIVERSITY

CCD detectors have their genesis in techniques of image intensification and the TV-type detection dating back to the late '60s. A that time, George Reynolds, a man whose ideas were typically ahead of their time, realized that an external scintillator and the image intensifier methods he had been applying to studies in high energy physics at Princeton University could also be used for crystallography. In 1968, in collaboration with G.F. Elliott and Bob Langridge, George set up an image-intensified camera to record the diffraction from a crystal of cacodylic acid (Figure 1b; [1]). The camera consisted of a

thin CsI:Tl scintillator crystal on the fiber optic input of a multistage image tube, the output of which was recorded on photographic film. Although the resulting pictures appear crude by modern standards, George was encouraged to find that he could acquire diffraction patterns hundreds of times faster than with x-ray film.

The use of image intensifiers for recording diffraction patterns was not new, having already been discussed by Bertin in 1953 [2]. The key technical development used by George, and about the same time by Uli Arndt and B.K. Ambrose [3] at the MRC laboratory of Molecular Biology in Cambridge, was the development of image tubes with fiber optic input windows. This allowed an external luminescent screen to be coupled to the image tube photocathode without the inefficiencies of lenses and with acceptable resolution.

In general, electro-optical x-ray detectors can be modeled as a sequence of sequential elements: An energy converter which stops the x-rays and produces a (typically) larger number of more readily manipulated quanta which are conveyed to a gain element, which multiplies the quanta, and a readout device to record the amplified image. In Figure 1, the converter is a scintillator, the gain element is a magnetically focussed image tube and the recording device is a photographic film camera. Let the number of photons produced in the scintillator be N_P, which are conveyed with efficiency C_{PI} to the intensifier, of gain, G. The output of the intensifier is then the product $N_P C_{PI} G$ photons/x-ray stopped. If this signal is coupled with efficiency C_{IS} to an image recorder of quantum efficiency, Q_S, then the signal, N_S, in the recorder is $N_S = N_P C_{PI} G\, C_{IS} Q_S$. George's detector produced about 300 developed film grains per CuK_α X-ray stopped, as compared to 1 grain/x-ray in x-ray film. This is why the diffraction could be recorded so much faster than on x-ray film.

George enlisted two good graduate students, Tom Minor and Jim Milch to develop the system. By the time I joined the group as an incoming graduate student in 1972, they had nearly assembled the apparatus shown in Figure 2 and set about to record a full lysozyme data set, work which was to be Tom's Ph.D. thesis dissertation [5]. With the crystallographic help of Tony Wright in Bob Langridge's lab in the Biochemistry Department, they were able to record 130 rotation pictures, spanning 280° of rotation in just over 6 hours [6]. In 1973, this was pretty remarkable. Unfortunately, when the intensities were compared against diffractometer data recorded by D.C. Phillips, the intensities didn't match, which was a big disappointment and led many to dismiss the work. It was later realized that there were two nearly identical crystalline forms of lysozyme, and the Princeton and Phillips data were not on the same form. It was hardly surprising that the intensities didn't match!

Work continued on the intensifier-film system and resulted in Jim's Ph.D. thesis [7] on leucyl-rRNA-aminoacyl ligase. But it was clear that the weak point in the system was the film. Processing hundreds of films was no fun and, worse, film has only a small linear dynamic range. A better way to record the intensified signal was needed. Our goals were to achieve three benchmarks: First we wanted quantum-limited single photon performance, in order to compete with the wire counter technology being developed by Xuong and colleagues in San Diego [8]. This meant that the signal per x-ray should be at least as great as the noise in reading out the signal. Second, our frustration with film led us to want a large dynamic range, which meant that the ratio of the TV signal at saturation to the zero x-ray dose readout noise should be as large as possible. Finally, we wanted good resolution, which meant designing the system so the Point Spread Function (PSF), e.g., the optical spreading of a point-like incident signal, was as narrow as possible. It was important that the PSF remain narrow down to many decades from the peak intensity, e.g., be both narrow at full width at half maximum and at 0.1% of maximum.

TV cameras were an obvious way of recording the intensified images, but most available TV cameras were noisy, nonlinear and had too low a dynamic range or didn't work well at very low frame rates. George Reynolds had spent a sabbatical year in Cambridge in 1974 and had worked with Uli Arndt on intensified detectors using TV recorders. George returned to Princeton convinced that the image isocon TV tube used earlier by Arndt (e.g., see [9]) was too noisy and nonlinear for the task. Fortunately,

there were superb astrophysics groups at Princeton from whom we learned a lot about emerging electronic TV-type sensors. Astronomical imaging bore many similarities to the x-ray problem, namely, the signals were weak and required long exposures and there was a need for wide-dynamic range, quantitative recording. Crane and Davis [10] at Princeton published an excellent paper on silicon diode vidicon (SIV) tubes which convinced us that this would work as a film replacement. The system George, Jim and I assembled (Figure 3; [11]) acceptably met our three benchmarks. My Ph.D thesis was on the assembly, characterization and use of this system on diffraction from membranes extracted from the rod outer segments of photoreceptor cells [12]. This detector was in dedicated service in my lab for another decade and was the primary data acquisition device on many scientific papers. In 1988 we retrofitted the detector with a commercial CCD camera; it continues to be used to this day [13].

About this time, the large area Silicon Intensified Target (SIT) vidicon became available. The SIT consisted of a reducing intensifier in which the accelerated photoelectron image was electrostatically focussed onto the target of an attached SIV. These tubes were built to meet the needs of the government to automatically track the rapidly proliferating amount of satellite and rocket debris orbiting the earth. Although these tubes were incredibly expensive, the government contract called for a tight specification on uniformity of response. Our detectors were never uniform enough for our purposes, so we always calibrated them and digitally post-corrected the images for nonuniformities. In consequence, SIT tubes which were rejects from the government program were good enough for us and were obtainable from RCA at prices, though high by our standards, were within reach.

Our detector research was mostly supported (and still is!) by what is now called the Office of Biological Research in the Department of Energy (OBER-DoE). The people in OBER-DoE recognized the potential of synchrotron radiation (SR) and foresaw the need for advanced detectors. We had become aware of SR largely as the result of a conference on the research applications of synchrotron radiation at Brookhaven National Lab in 1972 [14], and were very excited by the possibilities, especially for biological physics work. In consequence, as we built detectors, we were simultaneously thinking about SR experiments we wanted to perform with the detectors. Following the philosophy of George Reynolds, the detectors were never built as an end unto themselves, but rather always as tools with which to perform specific studies of interest.

Jim Milch (who by the mid- ‘70’s was an Assistant Professor in the Princeton Physics Department), George Reynolds and I started assembling a 40 mm SIT camera which Jim was going to take on a sabbatical to the DESY synchrotron lab in Hamburg, Germany. Jim was interested in using synchrotron radiation to study muscle. Jim and the SIT detector made an impression at DESY and resulted in a number of publications [15], [16], [17]. After a year, Jim and the SIT returned to the U.S. The SIT was soon used on experiments at SSRL [18].

We next constructed a larger, 80 mm SIT detector (Figure 4; [19]). Notice that with each new device the performance got a little bit better. Figure 5 shows a 12 msec exposure of a lipid phase, part of a time-resolved temperature-jump experiment on phase transitions in lipid systems taken at X10A at the NSLS [20], [21]. This detector also continued in service at Princeton University for another 15 years and was the key instrument for many papers and Ph.D. theses. A clone of the detector was fabricated at the University of Pennsylvania for Kent Blasie and Gerd Rosenbaum for use at X9 at the NSLS. This device was also used at SSRL [22].

The period 1968 through 1993 involved the development of many aspects of detector systems, by several research groups, which would prove to be the foundation for the CCD detectors now in use. For our group, these included research and development on

- Better phosphor materials and better phosphor screens [23] - [25];
- Improved fiber optics and better ways of testing fiber optics [26];
- Methods of coupling fiber optics to phosphors, other fiber optics and sensors [13]; [26];

- Use of cooled, slow-scan (narrow bandwidth) operation and low-noise FET amplifiers [4]; [11]; [19]; [27] - [32];
- Methods of testing detectors and calibration procedures [4]; [33]; [34]; and
- Much software development.

The need for a standard set of quantitative criteria for evaluating x-ray detectors was particularly pressing [4]; [33]; [34]. The fact that one could couple a phosphor to a high gain image intensifier and easily see single x-rays stimulated led many investigators to the incorrect conclusion that building a quantitative x-ray detector would be straightforward. Unfortunately, most such devices, while arguably quantum limited, suffered from problems which precluded their practical use. The list of possible problems was lengthy, and included effects such as dark currents high enough to severely limit the exposure time, false events, unacceptable noise, poor spatial resolution, geometric distortions, instabilities which precluded practical calibrations, short-lived or unavailable parts, etc. Very early on our group began defining test procedures to quantitatively compare our various detector designs [33]. In a 1982 symposium and workshop on crystallographic detectors we proposed adoption of a uniform set of criteria to measure detector performance [4]. There was a frustrating reluctance among detector designers to adopt any uniform set of test criteria. There was an equally frustrating reluctance of the crystallographic community to test detectors in any absolute way. Rather, there was a tendency to simply determine if the detector was better or worse than whatever one was used to using. The problem with this approach is that it does not provide an evaluation of the potential of the detector. Even so, inspection of detector papers written over the ensuing years shows that most of the criteria were eventually adopted by much of the detector community.

3. OTHER DETECTOR EFFORTS

The Princeton group was not the only group developing electro-optical detectors for synchrotron science. Uli Arndt and co-workers at the MRC in Cambridge, England had started working on intensified x-ray detectors about the same time as George Reynolds and were in frequent communication with us. The approach Uli took was completely different than ours [35]; [36]. The big debate in the field at the time was whether it was preferable to operate the vidicon in slow or fast scan mode. Fast-scan mode was similar to normal TV operation in which the tube is read out continuously at rates of, say, 10 Mpix/s. This means the preamplifier had to have a wide bandwidth which admitted much of the noise spectrum and resulted in high noise. It was still possible to be low-dose quantum limited, but it required very high gain image intensification to pump up the signal from each x-ray so as to be above the noise. The larger signals per x-ray also meant that the dynamic range/pixel/read out was reduced. An advantage of fast-scan was that the short time between read outs of the camera left little time for dark current accumulation, so the vidicon could be operated at room temperature.

By contrast, our group chose to follow the lead of the astrophysical community and use cooled, slow-scan operation. In this mode, the detector is operated in a cycle involving an integration period followed by a slow read of the camera. The vidicon is read out slowly (e.g., 50 kpix/s) via a narrow bandwidth preamplifier, thereby dramatically decreasing the noise and increasing the dynamic range/read-out. The lower noise needed less image intensification to achieve single x-ray quantum limited performance. It took almost 20 seconds to read out the camera and raster scan the vidicon target to prepare it for the next integration period. Then the camera read out was halted and the next exposure was allowed to accumulate on the vidicon target for periods of time that ranged from a fraction of a second to tens of minutes, depending on the intensity of the x-ray signal. Because it was necessary to integrate and store the signal on the vidicon target for long periods of time, the vidicon was cooled to -40 C to lower the dark current and signal leakage. Although slow- and fast-scan modes of operation were completely different, they used exactly the same vidicon tubes, which caused no end of confusion to the uninitiated.

George Reynolds had spent a sabbatical year in Cambridge in 1974 and had worked with Uli Arndt. George returned convinced that slow-scan was the preferred mode. Uli kept working away at the fast scan system, which eventually evolved into the FAST detector system vended by Enraf-Nonius [36]. In the FAST system, the data continuously streaming from a SIT tube was digitized to 8 bits and summed into RAM organized as a huge rotating shift register clocking in synchrony with the target scan. A number of FAST systems were sold. However, the system was bulky and suffered from a wide low-level point spread function.

Yet another fast-scan approach, developed by Ken Kalata at Brandeis University, involved sufficiently large image intensifier gains that each stopped x-ray left a spot well above the noise in the vidicon image [37]; [38]. As the image was read out, dedicated electronics would search for the spot and compute the centroid, the coordinates of which were then added into digital memory. Because the centroid could be determined to sub-pixel accuracy, this system had incredible resolution and was a very low-noise photon counter. Its weakness was that it depended on non-overlap of x-rays during a frame period, which was on the order of 10 ms. This imposed a severe local count-rate limitation which precluded use for most SR applications. The detector also could be operated in an analog mode in which the integrated signal was run through an analog-to-digital converter and the digitized signal allocated to memory. In the latter mode, the detector was, in principle, similar to the Arndt design. To add to the confusion, this system also used a SIT vidicon, so when SIT x-ray detectors were discussed it was necessary to say whose SIT detector was involved.

The fundamental weakness of the fast-scan approaches was the high read out noise necessitating high gain multi-stage image intensification. Although these methods worked in principle, image tubes were delicate, expensive, generally had small input areas, were susceptible to magnetic fields and required very high voltage power supplies. The slow-scan approach allowed the use of a single stage of image intensification and, with the eventual introduction of very low noise CCDs, elimination of the intensifier altogether.

Other, completely different detector methods were also being developed for SR use. The Multi-Wire Proportional Counter (MWPC) so successfully developed by Xuong et al. [8] for home laboratory use inspired many laboratories to develop MWPCs for SR use. A good example is the spherical drift MWPC at LURE [39]. These detectors had the advantages of low-noise photon counting operation and fast readout. The disadvantages included a local count-rate limitation, parallax effects stemming from the thickness of gas (generally Xe) needed to effectively stop the x-rays and low stopping power at higher x-ray energies. The local count-rate limitation generally arose from the time required to encode the position of the event with a small number of channels of read out electronics. This limitation could be mitigated with segmentation of the detector and a corresponding increase in the number of parallel readout channels, but at the cost of increasing complexity. The great complexity of MWPCs, which frightened away vendors, is probably their greatest limitation.

In the mid-1980's the Image Plate (IP) or storage phosphor appeared [40]; [41]. IPs were a tremendous development and catalyzed an enormous increase in SR utilization. In an IP, a phosphor (generally $BaFBr:Eu^{+2}$) is used to analog store the x-ray image. X-rays excite deep trap states with very long (hours to days) lifetimes. The trap states can be de-excited by photostimulated luminescence with red light and results in the emission of blue light, the intensity of which is proportional to the stored x-ray dose. In practice, the plate is exposed and then, post-exposure, is scanned with, for example, a HeNe laser. An optical interference filter allows rejection of scattered laser light and recording of the photostimulated signal with a photomultiplier.

The IP had advantages of a large size, lots of pixels, good signal to noise ratio, a large dynamic range (in principle), and relative robustness. Most importantly, the technology was simple enough that several vendors quickly appeared. The disadvantages of the IP were the need for a relatively slow readout cycle, difficulty erasing the plates, low-level systematic effects, and dynamic range limitation arising from the IP scanners. But the IP was a huge advance over previous SR detector methods and

continues to be a popular and effective SR detector. It is slowly yielding to CCD detectors (see below) which are more sensitive and convenient for the most demanding macromolecular applications.

4. CCD DETECTORS

The shift from vacuum tube TV imagers to CCDs was an incremental step in the progression of imager improvements in x-ray detectors. Why then, has the CCD-based detector had so much larger a practical impact than prior imager improvements? The primary answer is simply that CCD noise levels were sufficiently low to eventually allow elimination of the need for image intensification. By the late 1960's phosphor efficiencies were already within a factor of two of theoretical maximums (e.g., see [42]. Although fiber optic taper technology improved with respect to image quality and maximum size, by the mid-1970's tapers also were already near theoretical limits [43]; [44]. Vacuum tube vidicon (e.g. SIV) quantum efficiencies were also already near unity. Thus, almost a quarter century ago the number of luminescent photons that could be delivered to the imager by a phosphor-fiber optic taper combination were already near a theoretical maximum. This number was in the range of 5 – 50 electron-hole pairs per diffraction x-ray for demagnification factors of 5 - 3, well below the noise level of several thousand electrons/pixel typical of vacuum tube vidicons. Hence, as described in Section 2, image intensification between the phosphor and the imager was required for good signal to noise ratio. By contrast, CCDs with read noise levels in the range of 5 - 20 electrons soon became available, thereby allowing signal-to-noise levels on the order of unity without image intensification. This was an enormous improvement because image intensifiers, remarkable though they are, have drawbacks of delicacy, bulk, expense, instability, sensitivity to magnetic fields, requirements for several high voltages, nonlinearity, and difficulty of manufacture with large input areas.

Work on CCD detectors in my Princeton laboratory started in 1984. By this time I had been on the Princeton Physics Department faculty for about 7 years and had become the leader of the detector group started by George Reynolds. George was preparing for the retirement at age 70. (Formal "retirement" at age 70 was required back then. However, George remains active and involved in lab research even today). By the mid-1980's a core group consisting of George, Mark Tate (then a graduate student), Eric Eikenberry (from nearby Rutgers University), and me were hard at work on new detectors. We had considerable help from John Lowrance, an engineer formerly of the Princeton University Astrophysics Department. John left Princeton University to form a small company, Princeton Scientific Instruments, which specialized in making CCD controllers for large telescopes.

By the early 1980's the astronomical community had demonstrated the clear superiority of CCDs to vacuum tube imagers when the CCDs were operated in a cooled, slow-scan mode. However, in astronomical applications the image was typically lens coupled onto the CCD, in which case, the small CCDs then available were often adequate. By contrast, x-ray detectors consisting of a phosphor directly coupled to the CCD required the development of both large area CCDs and methods of attaching the fiber optics. In consequence, our early CCD detectors still utilized image intensification [29]; [30]. Elimination of the intensifier was feasible if image reduction was not needed [26], as was the case for the microtomography application developed for use on the Exxon beam lines at the NSLS [31], because of the high efficiency of image magnification (as opposed to demagnification; see [26]).

In 1989, Don Bilderback (CHESS) and I were both attending the Synchrotron Radiation Instrumentation conference in Tsukuba, Japan. We both had signed up for a tour to the beautiful site at Nikko and, en route, got into a conversation about assembling a directly coupled CCD detector and testing it at CHESS. We decided to try it. With the help of John Lowrance, our group assembled a detector consisting of a phosphor on a 1:1 fiber optic blank, which was directly coupled by optical coupling oil to the surface of a Tek 2048 x 2048 pixel CCD. Figure 6 and Table 1 shows the remarkable performance of this device [32]. These results convinced us that directly coupled CCDs were desirable. Comparative tests also convinced us that CCDs were superior to image plates, the then current darlings at storage ring sources.

By 1990 our Princeton group was designing fiber-optically-coupled CCD detectors both with and without image intensifiers. The big problem at the time was obtaining fiber-optically-coupled CCDs that could be operated at low temperatures without failure of the fiber-optic to CCD bond. Thomson-CSF was willing to quote on suitable CCDs, which had low noise and were guaranteed to low temperatures. Thomson had a 512x512 pixel CCD with imaging area about 1 cm across and a chip twice as large in the final stages of development. We wanted a minimum input area 5 cm across, necessitating 5:1 demagnification for the smaller CCD. We calculated that a detector using the smaller CCD would need at least one stage of image intensification to be low dose quantum limited, whereas the large chip could be run without intensification. In the end, we decided to procure both CCDs and build two detectors, one with and one without intensification. Relevant information for the nonintensified detector is in Figure 7.

The detectors were built primarily for use with our rotating anode x-ray generator for various SAXS experiments in which we were engaged. We were also encouraged to test the detectors for macromolecular crystallography by Don Bilderback, now Associate Director of CHESS and by Steve Ealick. Steve had arrived at Cornell to direct MacCHESS, the macromolecular resource at CHESS, after Keith Moffat, the previous director, had left for the University of Chicago. The first protein crystallography detector runs at CHESS occurred in September 1992 with the intensified CCD detector, and yielded high quality data at the old CHESS A1 station. Steve and I were thrilled to watch one image after another roll off the detector and instantly became convinced that this technology would change the way macromolecular users would acquire data at synchrotron sources. Our tests also emphasized the importance of incorporating x-ray energy- and angle-dependent effects in the calibration procedures [24]. In the spring of 1993, we returned with both the intensified and nonintensified CCD detectors, just in time to acquire data to show at the MacCHESS grant renewal site visit. My intention was to use the proven intensified version with the newer nonintensified version as a backup, but on the trip to Cornell Mark Tate argued that we should first try the nonintensified version. As it turned out, the nonintensified version performed flawlessly and when we returned to Princeton we realized that the intensified version had not even been unpacked.

Steve Ealick had arranged for time on the CHESS F1 station a day before the MacCHESS grant site-visit. In order to have something to show, Steve had asked Wladek Minor to bring ϕX174 virus crystals from Michael Rossmann's Purdue University lab and David Rogers to bring tomato bushy stunt virus crystals from Steve Harrison's lab at Harvard. I will never forget the excitement on people's faces as the first images rolled off one after another (Figure 8). The raw image quality was sufficiently good that I had to keep reminding people that the data should not be analyzed until the images had been fully calibration processed. Afterwards, we rolled the entire detector and the associated computer into the CHESS conference room to show the site-visitors the first macromolecular data acquired just hours earlier with this new detector. Everyone was impressed at the quality of the images and could hardly believe that the actual detector area was only 5 cm across.

I was soon convinced to loan the "1k detector", as the unintensified detector came to be called [45], to CHESS for a period of time. Reports soon began filtering back about fabulous data acquired with the 1k. Wladek Minor used it to acquire a 1.4 Å resolution data set on lipoxygenase, an 839 amino acid protein in a single evening. The data set consisted of 1.1 million observations and was 96% complete with a R_{sym} of 3.6%, which, at the time, was an astonishing accomplishment. CHESS soon had users insisting that they simply had to use the 1k to get their data. Whenever I inquired about repossession of the 1k I was persuaded that it was serving users so well that it would be a shame to remove it. The 1k is still operating faithfully at CHESS to this very day and has been the data collection instrument for many, many papers (e.g., for the early years, see [46] - [48]). I often joke that I found it easier to move to Cornell (which I did, as CHESS Director, in 1997) than to take the 1k back to Princeton.

In the meantime, our Princeton group was busy improving the speed of the calibration procedures and, with the help of John Lowrance, in making CHESS a larger, faster read out detector based on a 2048 x

2048 CCD. This detector was delivered to CHESS and soon was also being heavily used by the macromolecular community [49]. Interest in CCD detectors grew rapidly, catalyzed both by macromolecular results obtained at CHESS, at other synchrotrons with intensified detectors (e.g., see [50]). In addition, other CCD efforts utilizing phosphor screens coupled to CCDs via fiber optic tapers were soon to yield new macromolecular structures (e.g., see [51]).

One of the most important changes that occurred was that x-ray equipment vendors became interested in CCD detectors. This was highly welcome since it was obvious that small university groups could neither meet the rapidly increasing demand for CCD detectors, nor could they provide the requisite long-term support. Our original plans to fabricate a large detector from a mosaic of smaller CCD modules were abandoned when it became clear that this development would be performed by commercial vendors anyway. In retrospect, it is seen that the research which led to the now standard CCD detector configuration (e.g., a phosphor screen directly coupled to a cooled, slow-scan CCD via a fiber-optic taper, with post-calibration of the acquired images) had been essentially completed by 1991 and validated in practice with the 1k detector in 1993. From that point on, making bigger and better CCD detectors has been mostly a straightforward, although hardly trivial, development. Today a variety of CCD detectors are available from almost a dozen vendors.

5. PIXEL ARRAY DETECTORS

The CCD detector, in conjunction with fast freezing of proteins to mitigate radiation damage and constant synchrotron and beamline improvements, has enabled very rapid collection of macromolecular data. Data collection is no longer a rate limiting step for most protein structures. The popularity of CCD detectors is certain to grow over the coming years. Rapid data collection, when coupled with genomic methods which allow rapid modification and expression of proteins, is certain to have enormous impact science and technology.

What about the future? Although prognostication is always dangerous, it is safe to note that several groups around the world, including my own in the Cornell Physics Department, are researching Pixel Array Detector (PAD) technology (e.g., [52] - [57]). PADs are solid state devices in which x-rays are stopped in a semiconductor layer and the relatively large resultant charge is processed in an attached CMOS electronics layer. The nonlinearities, distortions, speed and resolution limitations of phosphors and fiber optics are avoided, as these components are not needed in most PAD designs. Typically, each pixel of a PAD has its own processing electronics, which affords tremendous flexibility to configure detectors for custom x-ray applications. PADs promise to have many advantages over CCD detectors and may eventually replace them, just as CCDs are displacing earlier detectors. And, of course, other detector technologies (amorphous silicon imagers, superconducting granule detectors, etc.) are being researched. The benefits of development of these devices will certainly continue to be reaped by the synchrotron user community.

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TABLE 1
Summary of the CCD Detector Parameters

CCD	TEK 2K, 2048 x 2048 pixels
Pixel Size	27 μm x 27 μm
Phosphor	Gd_2O_2S, 8.4 mg/cm^2, 50 mm dia.
PSF	< 50 μm, FWHM
Sensitivity	16 e^-/x-ray, ^{55}Fe
Saturation	4 x 10^4 x-ray/pixel
Dynamic Range	3 x 10^4
Dark Current	13 e^-/pixel/s @ -42 · C (0.8 x-ray/pixel/s)
Dark Current Noise	4.8 e^-/pixel/s$^{-1/2}$ @ -42 · C (0.3 x-ray/pixel/s$^{-1/2}$)
Readout Noise‡	22 e^- (1.4 x-ray)
Linearity	Excellent
Distortion	< 0.35 pixel
"Zinger" Rate	4 x 10^{-7}/pix/s on phosphor 6 x 10^{-8}/pix/s off phosphor
Readout Time	110 s

‡Includes some dark current because of the readout time. From [32]

FIGURE CAPTIONS

Figure 1. (a) Arrangement of the detector elements used by G. Reynolds [1] in 1968. The number of quanta at various points along the detector chain are indicated and explained in the text. (b) A 1 second image of the diffraction pattern of cacodylic acid acquired with the system. (c) A 5 minute image of the same crystal as recorded on x-ray film.

Figure 2. (a) Schematic of the automated imaging diffractometer described in [6]. 150 second lysozyme diffraction patterns acquired with this system are shown in (b) and (c).

Figure 3. Schematic arrangement of the detector components used in [11]. The quantum limited criterion is given by adjusting the image intensifier gain so that the single x-ray signal in the SIV vidicon is equal to the single pixel readout noise of about 6000 electrons. True quantum limited performance required an even higher signal to noise ratio because the signal from each x-ray is spread over several pixels due to the system point spread function. This was easily compensated for, if required, by increasing the gain of the image intensifier.

Figure 4. A detector based on a SIT vidicon had improved performance over detectors with lens-coupled intensifiers [19]. Compare to Figure 3.

Figure 5. A 12 msec diffraction pattern of a lipid-water phase during a temperature-jump experiment at the NSLS [21]. (a) shows the diffraction pattern and (b) shows a radial integration through the diffraction pattern, clearly indicating the (1,0), (1,1) and (2,0) reflections of a hexagonal (H_{II}) lipid phase.

Figure 6. (a) A 1 pixel wide scan through a line of reflections of a diffraction image from a gallium arsenide/gallium aluminum arsenide multilayer crystal taken with a 2k CCD detector [32]. The system shows remarkable resolution and the FWHM of many of the peaks are only a single 27 micron pixel wide. (b) A diffraction pattern recorded on an image plate system shows a much poorer PSF. In the image plate system, the pixels were 100 microns wide, so it was necessary to increase the specimen distance relative to the CCD detector.

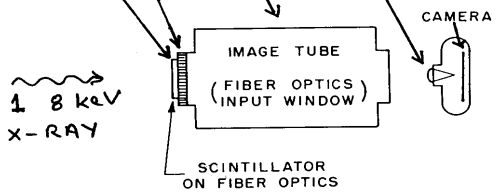
Figure 7. Schematic of the "1k" CCD detector [45]. A single 10 keV x-ray signal to single pixel noise ratio of greater than 1 could be achieved without image intensification.

Figure 8. A 0.2° oscillation diffraction image of tomato bushy stunt virus acquired in a 40 second exposure on the CHESS F1 line with the 1k CCD detector. The actual detector image is 5 cm wide. From [45].

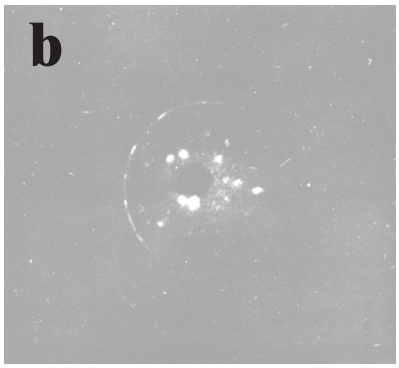
a

$$N_P \times C_{PI} \times G \times C_{IS} \times Q_S = N_S$$

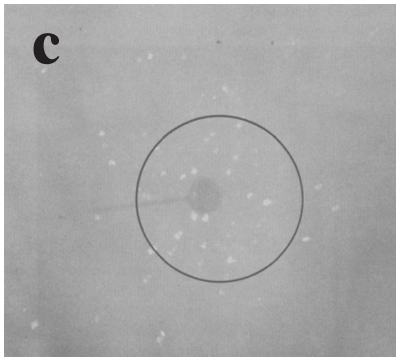
$$200 \times 0.3 \times 40{,}000 \times 0.027 \times 1/200 = 300$$

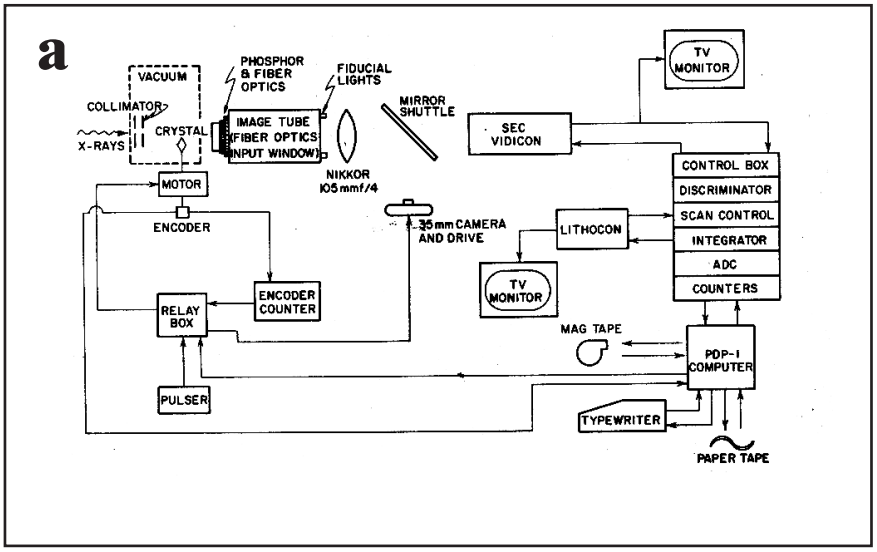


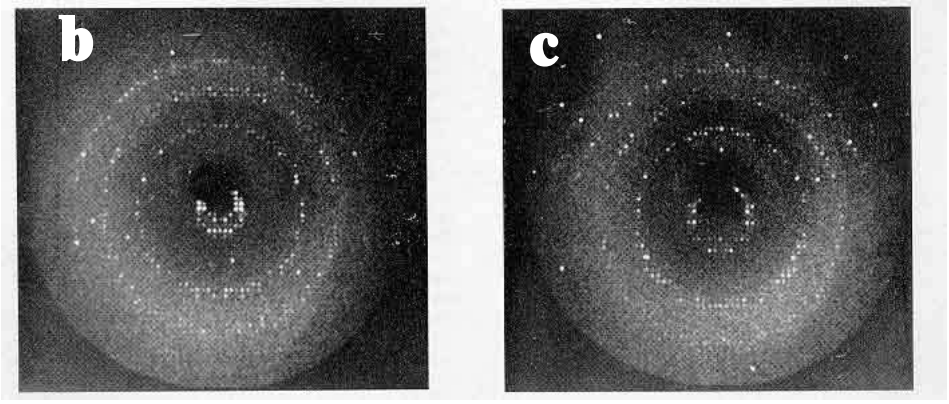
b



c




a
VACUUM
COLLIMATOR
X-RAYS
CRYSTAL
PHOSPHOR & FIBER OPTICS
IMAGE TUBE (FIBER OPTICS INPUT WINDOW)
FIDUCIAL LIGHTS
NIKKOR 105mmf/4
MIRROR SHUTTLE
SEC VIDICON
TV MONITOR
CONTROL BOX
DISCRIMINATOR
SCAN CONTROL
INTEGRATOR
ADC
COUNTERS
MOTOR
ENCODER
35mm CAMERA AND DRIVE
LITHOCON
TV MONITOR
ENCODER COUNTER
RELAY BOX
MAG TAPE
PDP-1 COMPUTER
PULSER
TYPEWRITER
PAPER TAPE


b
c

1) **Quantum Limited Criterion**

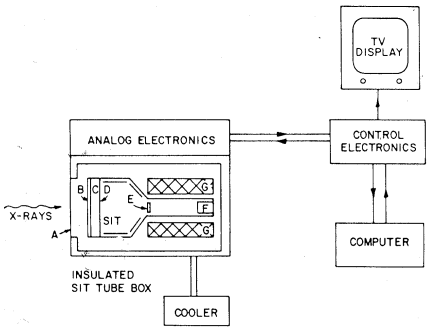
   N_S (# e^- / X-ray) = σ_{Detec} = 6000 e^-/pix

$$N_P \times C_{PI} \times G \times C_{IS} \times Q_S = N_S$$
$$200 \times 0.6 \times G \times 0.004 \times 0.8 = 6000$$
$$\Rightarrow G = 16{,}000 \quad \text{(Easy!!)}$$

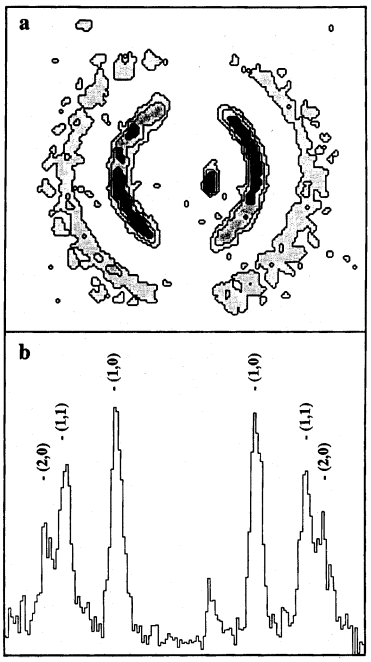
2) **Dynamic Range / pix** $= \dfrac{4.5\text{x}106\ e^- / \text{pix}}{6000\ e^- / \text{pix}}$

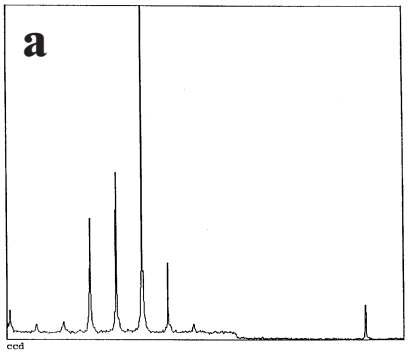
$$= \boxed{750}$$

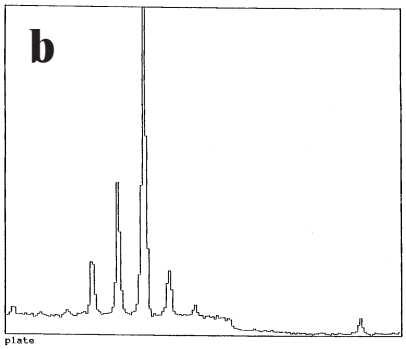
3) **Format: 256 x 256 pix**
   FWHM PSF = 3 pix

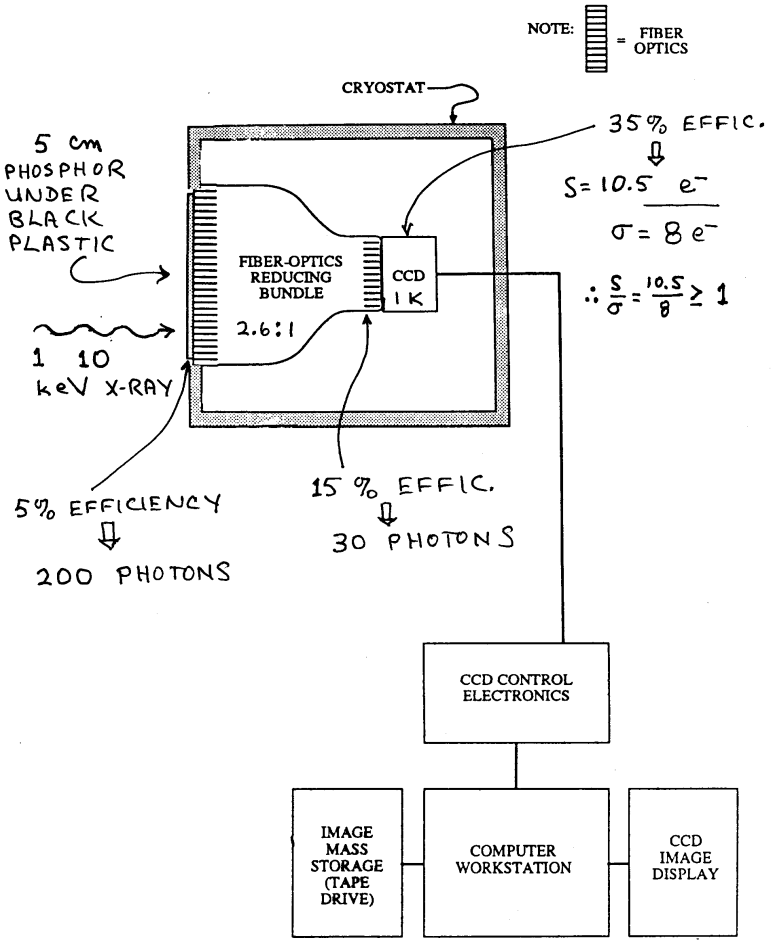


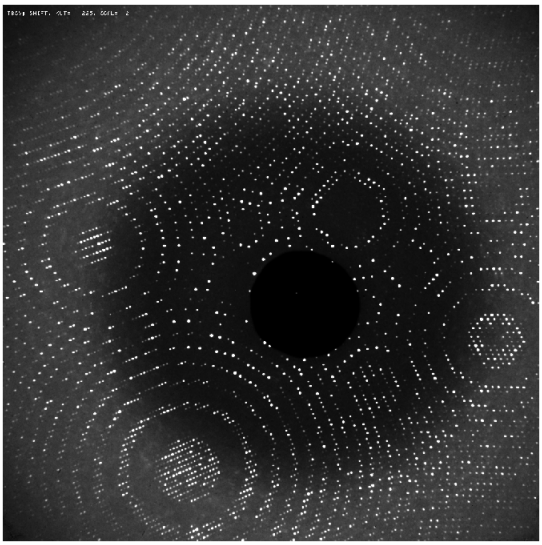
- $\sigma_{Det} \cong$ **4,000 e$^-$/pix** $<$ N_S**=10,000 e$^-$/x-ray**
- **Dynamic Range = 1,000**
- **Format: 256 x 256 pix**
- **FWHM PSF = 1.7 pix**


a
b
- (2,0)
- (1,1)
- (1,0)
- (1,0)
- (1,1)
- (2,0)


a
ccd


b
plate


NOTE: = FIBER OPTICS
CRYOSTAT
5 cm PHOSPHOR UNDER BLACK PLASTIC
35% EFFIC.
S = 10.5 e⁻
σ = 8 e⁻
∴ S/σ = 10.5/8 ≥ 1
FIBER-OPTICS REDUCING BUNDLE
2.6:1
CCD 1K
1 10 keV X-RAY
5% EFFICIENCY
200 PHOTONS
15% EFFIC.
30 PHOTONS
CCD CONTROL ELECTRONICS
IMAGE MASS STORAGE (TAPE DRIVE)
COMPUTER WORKSTATION
CCD IMAGE DISPLAY


TRIS: SHIFT. CLT: 225. SCALE: 2

Questions

Frank Rotella: Would you comment on amorphous silicon area detectors: their future development and roles in crystallography and imaging?

S.M. Gruner: Amorphous silicon detectors are being intensively developed for radiographic applications. Amorphous silicon has advantages of ease of fabrication over large areas and lots of pixels. However, amorphous silicon also has significant materials problems which makes it difficult to adapt for crystallography and demanding quantitative imaging applications. These problems include a high intrinsic noise and read out lag (i.e., not all the signal is read out in one stroke). Much more research will e needed to determine if these problems can be overcome in a cost effective manner.