

# Small molecule systems based on hybrid pixel array technology

## XtaLAB P200



### 1. Introduction

For the expert small molecule crystallographer, where a flexible configuration is required, Rigaku offers the XtaLAB P200 chemical crystallography system. The XtaLAB P200 represents a state-of-the-art chemical crystallography system with its incorporation of the DECTRIS PILATUS 200K hybrid pixel array detector (HPAD). The XtaLAB P200 can be configured with molybdenum (Mo) radiation, copper (Cu) radiation, or a combination of the two. With a true photon counting detector, the XtaLAB P200 is the perfect choice of X-ray diffractometer for both day-to-day routine crystal structure determinations and the more challenging high-resolution electron density studies.

### 2. Features of PILATUS 200K hybrid pixel array detector

#### 2.1. Direct detection of X-rays

The technology behind the PILATUS 200K is dramatically different from what is used in phosphor-based CCD detectors and phosphor-based CMOS detectors. In phosphor-based detectors, X-rays are converted to light, which then travels through a glass stub or taper and finally reaches a CCD or CMOS chip where it is accumulated until read (Fig. 1). The final step in the signal processing chain is an analog to digital conversion. Each step in the detection process adds to the noise of the signal and hurts the ability to measure weak signals.

With a hybrid pixel array detector, the X-rays are measured directly with a solid-state sensor (Fig. 2). Each X-ray photon that hits the detector creates a large number of electron-hole pairs, with the charge being

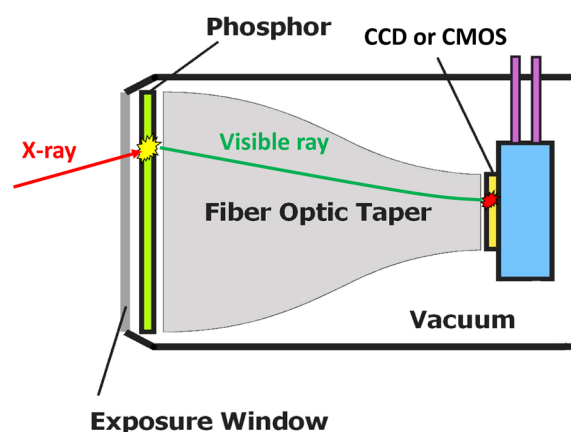


Fig. 1. Principle of a phosphor-based detector (CCD or CMOS).

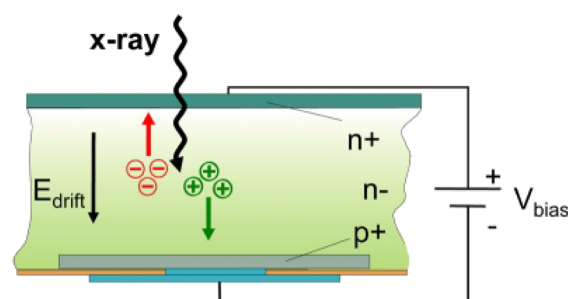


Fig. 2. Principle of direct detection of X-ray photon in a solid-state sensor.

directly transferred to the CMOS chip and measured without the need for analog to digital conversion. HPAD detectors feature very high dynamic range, extremely

low noise, and hence achieve optimal signal-to-noise ratio at short readout time and high frame rates.

## 2.2. Extremely low noise

The benefits to the chemical crystallographer are very significant. The low-noise characteristics of the detector mean that the ability to measure weak reflections accurately is improved. This can be seen in the measurement of higher resolution reflections for weakly diffracting crystals. A PILATUS 200K detector is the perfect device to optimally collect weak diffraction and improve the success of structure solution.

## 2.3. True shutterless operation

In addition to the outstanding low-noise characteristics, the PILATUS 200K allows you to collect data very quickly without having a negative impact on your data quality. The PILATUS 200K is a photon counting device, which means that it does not integrate photons before being read out. There is essentially no deadtime during readout so the most efficient way to collect data is to open the shutter, spin the crystal and measure data. Each shutter open/close operation, coupled with an oscillation axis start/stop, introduces error into the data. Shutterless data collection removes those errors as well as removing the deadtime from the experiment. The result is better quality data in a shorter period of time.

## 2.4. Excellent point spread function

A Point spread function (PSF) is often used as a means of quantitatively characterizing the performance of an imaging system. The PILATUS 200K detector has a very sharp PSF (smaller than one pixel), which means that reflections are sharper and easier to resolve.

Closely spaced signals, even of largely differing intensity, can be accurately resolved and measured. Sharper signals reduce overlap with scattering or other background intrinsic to the experiment, thereby improving the signal-to-noise ratio. Due to the direct conversion of X-rays into charge pulses, the PILATUS 200K detector spreads virtually no intensity between pixels. The PILATUS 200K detector enables optimally sharp images to be created, which are free of artifacts such as blur, intensity tails, blooming, or streaking typical of other detectors.

## 3. System configuration

With three different goniometer choices and ten different source choices, the perfect system can be configured to meet the needs of any research lab.

- **Choice of goniometer:** Three types of goniometers are compatible with the XtaLAB P200 system. With the four-axis partial chi or kappa goniometer, the open geometry vastly simplifies crystal mounting, alignment and positioning of low temperature devices while providing superior coverage of reciprocal space,

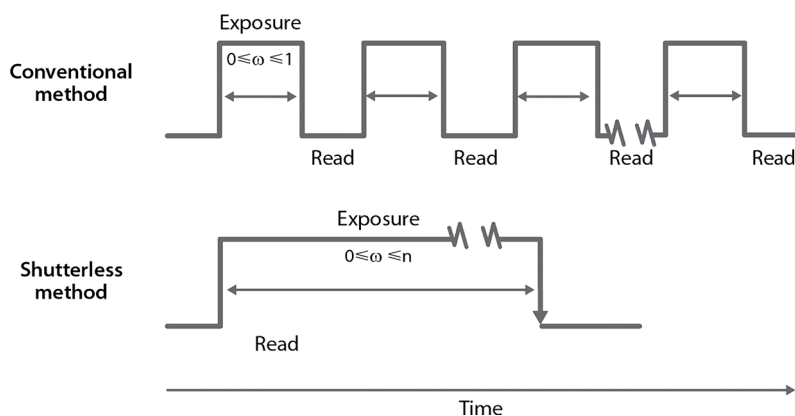


Fig. 3. Comparison of conventional data collection versus shutterless data collection.



Fig. 4. Lineup of goniometer.

even in the presence of tertiary equipment. However, depending on your requirements, a three-axis fixed-chi goniometer is also available.

- **Choice of X-ray sources:** Inherent to the unique flexibility of this system is a choice of X-ray sources, ranging from a high-frequency 3 kW sealed tube, to a MicroMax-003 microfocus sealed tube, to a 1.2 kW MicroMax-007 HF microfocus rotating anode and the industry leading 2.97 kW FR-X. Available optics range from a traditional graphite monochromator or high-performance SHINE optic to a VariMax confocal X-ray optic. For the MicroMax-007 HF and FR-X rotating anode generators, dual target anodes and dual wavelength multilayer optics are also available (Mo/Cu, Cu/Co, or Cu/Cr).
- **Complete software suite:** CrystalClear is the data collection and processing program package designed for single crystal data, underneath it runs the crystallographic package d\*TREK that works for any detector, many types of goniometers, and all kind of image formats. Based on Rigaku's easy-to-use flow bar user interface, CrystalClear walks the user through steps required to collect and prepare a data set for structure determination.

Structure solution and analysis are provided by Rigaku's CrystalStructure program suite. This flexible package includes multiple structure solution programs so that you can try various techniques when faced with difficult problem. Both the CRYSTLS and SHELX programs are supported so that you are ensured of working with software that is accepted around the world.

In addition to CrystalStructure, Rigaku provides a version of the popular small molecule package, Olex2. Olex is an easy-to-use program for small-molecule structure solution and refinement. It also includes many useful tools for structure analysis, archiving and report generation. All aspects of the structure determination and publication access are presented in a single, workflow-driven package. An active online user community ensures access to Olex2 experts.

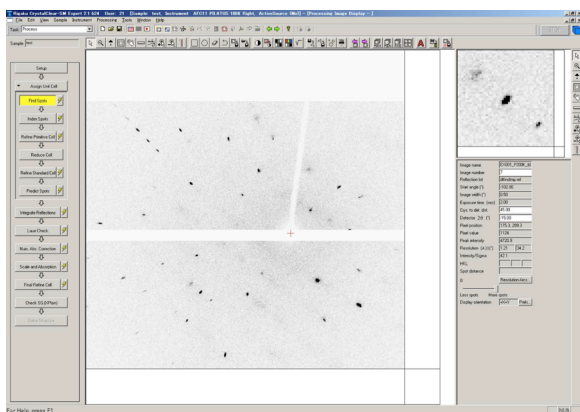


Fig. 5. GUI of CrystalClear data collection and processing software.

## 4. Applications

### 4.1. Data quality and speed

An X-ray system is only as good as the data collected and the structures solved and published. The current technologies of imaging plate, CCD, and phosphor-based CMOS detectors have all been proven to measure good, publishable data. Is there a better way? Can you measure weak data accurately? Can you improve data quality while actually reducing data collection time? The answer is "yes". With a system based on a direct detection detector, you can improve data quality and significantly improve data collection times.

Data sets were collected on a crystal of cytidine utilizing a CCD detector (Saturn 724HG) and a HPAD detector (PILATUS 200K). The crystal size was  $0.22 \times 0.22 \times 0.22$  mm and the exposure time was 4 sec/image. Two scans were performed to give P1 coverage.

As seen in Fig. 6, the merging statistics for the PILATUS 200K data are significantly better than from the data measured with the Saturn 724HG. This is exactly the sort of improvement that you would expect from an improvement in weak data measurement and the subsequent improvement in sigmas. R1 is the same for the two data sets, again this is to be expected from a well diffracting crystals where strong reflections will dominate. Finally, the full advantage of the PILATUS 200K detector can be seen in the data set that only took 17% as long to measure for equivalent or better data.

### 4.2. From small molecule to protein

The XtaLAB P200 system can be used for protein structure analysis as well as for small molecule chemical crystallography.

In the structure solution of insulin by sulfur single anomalous dispersion (S-SAD) phasing, having a tolerance to long-time exposure is required for a detector to detect a vanishingly small anomalous signal of the sulfur atom. Fig. 7 shows improved electron density maps of insulin calculated with the CRANK program after S-SAD phasing. The XtaLAB P200 MM007HF can provide a higher resolution map in an incredibly short time.

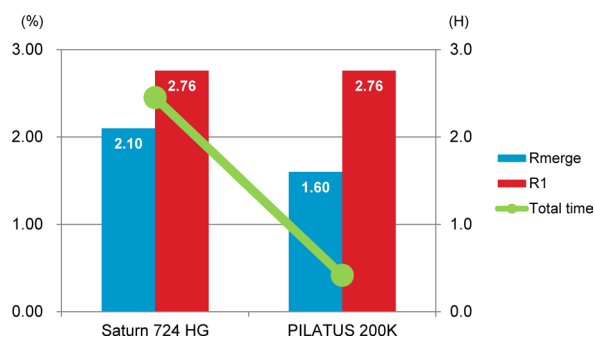
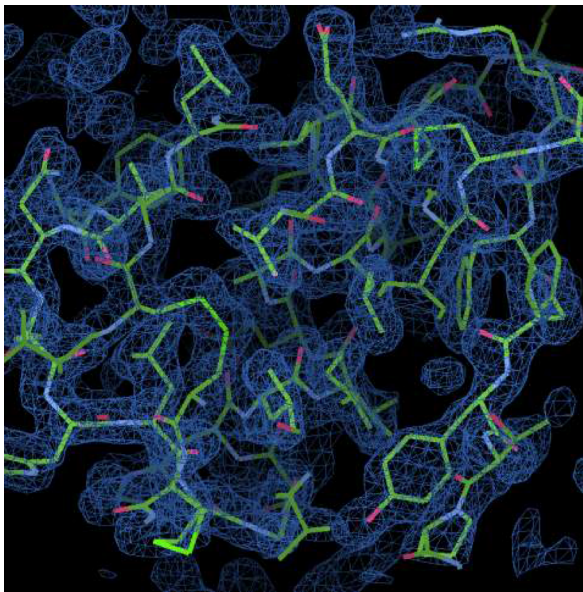


Fig. 6. Comparison of Saturn 724HG CCD and PILATUS 200K.



**Fig. 7.** Superposition of electron density map and molecular model from the XtaLAB P200 MM007HF.

**Table 1.** Data collection of insulin with the XtaLAB P200 MM007HF.

	XtaLAB P200 MM007HF
Oscillation	0.5°
Exposure time	4 sec
$\phi$ rotation	360°
Total time	48 min
Resolution	31.86–2.00 Å (2.07–2.00 Å)
$R_{\text{merge}}$	12.00% (47.10%)