White Paper

High Resolution & Novel Contrasts with PrismaXRM-300™ 3D X-ray Microscope

The PrismaXRM-300™ provides the leading resolution capabilities of any 3D x-ray microscope (XRM) / microCT on the market. In addition to its leading resolution, PrismaXRM offers exciting innovations that provide access to new modes of x-ray contrast, enabling breakthrough insight for a variety of applications, spanning from semiconductor to the life sciences and more.

This white paper will review the principles of XRM and PrismaXRM-300™'s design innovations

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High Resolution & Novel Contrasts with the **PrismaXRM-300™ 3D X-ray Microscope**

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Background: X-ray microscopy (XRM), provides non-destructive three-dimensional imaging of internal microstructure of samples, analogous to medical CT of the body - but performed at a much smaller scale. Laboratory XRM (also known as micro-CT) has developed substantially in the past two decades. Many systems are now reaching the limits of resolution achievable at high throughput.

Why was the PrismaXRM Designed? PrismaXRM is a novel 3D x-ray microscope developed to break through the visibility limits of the existing leading x-ray microscopes and to optimize performance for the most challenging XRM applications, such as in-situ imaging. To achieve the most advantageous imaging for each sample, the system provides two high performance configurations that may be selected by the user in seconds:

1. Ultrahigh resolution absorption micro-CT that **matches and exceeds** capabilities of other premium systems; and
2. A multi-contrast interferometer that **reveals hidden features** and substantially speeds up acquisition time of critical features (voids, orientations, cracks, etc.) to **within minutes**. This mode exclusively adds two new contrasts: Quantitative Phase™ and Subresolution Darkfield™.

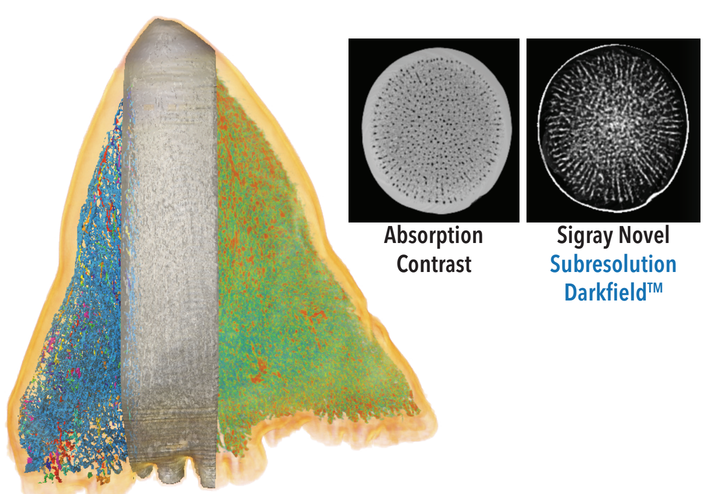


Figure 1: Novel multi-contrast x-ray microscopy, exclusive to PrismaXRM. Example of a shark tooth shown in absorption contrast (blue region), new Quantitative Phase™ (grey), and new Subresolution Darkfield™ (green). The contrasts are highly complementary: for example, darkfield reveals connectors between the pores not seen with absorption contrast.

The Physics: What is Absorption Contrast Imaging? To understand the difference between the two modes of the PrismaXRM, it is first important to understand absorption contrast, the most common method of imaging with x-rays and which is available in both modes.

Absorption contrast is the familiar form of imaging used by hospitals and dentists and is used by nearly all modern x-ray microscopes. It measures how many x-rays are absorbed by different regions of the object. If certain regions are more absorbing (e.g. lead), fewer x-rays will hit the detector compared to less absorbing regions, thus forming image contrast between regions. Although it is powerful, there are some drawbacks: absorption contrast can miss information encoded in other forms of contrast and can be time-consuming at high resolution (e.g. hours-long acquisition).

Novel Image Formation with Multiple Contrasts

Recent innovations are now enabling a new form of x-ray microscopy that acquires multiple contrasts simultaneously. As shown in Fig. 2, the contrast mechanisms (absorption, phase, and scattering) each affect the x-ray waves differently.

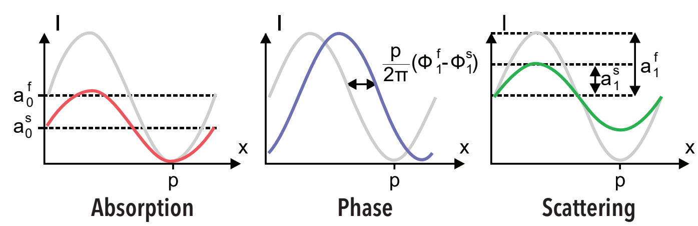
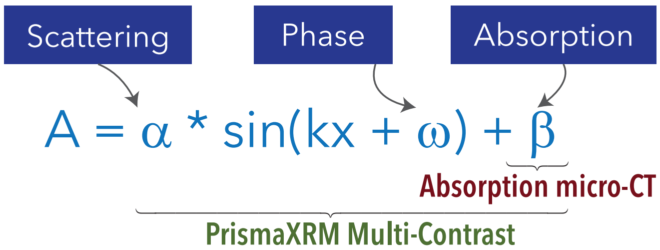


Figure 2: X-ray imaging is more complex than simply absorption alone: x-ray waves are affected by: absorption (reduces the amplitude), phase (shifts the wave), and darkfield/scattering (offset) caused by small features

Sigray's multi-contrast interferometer mode separates and measures each of these contrast mechanisms (absorption, phase, and darkfield/scattering) using an approach called grating-based interferometry (GBI). This approach measures a complete signal, described in Eqn. 1 below in which ***A*** is the measured pixel intensity during a grating scan, β is the attenuation (absorption), ω is the phase shift, α represents scatter (darkfield), ***x*** is the grating position, and ***k*** is the wavenumber.



Equation 1: *PrismaXRM gives the complete signal information, whereas absorption microCT/XRM only captures a portion of the information*

Eqn. 1 shows that absorption contrast represents only one component of a **far richer signal**. PrismaXRM measures all terms to provide a more complete description of the sample.

I. PrismaXRM Overview

PrismaXRM is the first X-ray microscope to extend conventional absorption micro CT to the **highest resolution and fastest throughput** available on the market, while additionally offering a completely new imaging technique that **simultaneously acquires multiple contrasts** (absorption, phase, and darkfield). With the click of a button, the microscope can be configured to collect absorption contrast or multi-contrast.

The system is enabled by several key innovations shown in Fig. 3, including a patent-pending multi-contrast approach, two x-ray sources (a nanofocus source optimized for absorption contrast and a patented microstructured source for multi-contrast imaging), and multiple detectors, including a novel direct detector for large field of view and a set of detectors that incorporate visible light objectives for variable magnification.

Specific advantages that PrismaXRM provides include:

1. Industry-leading **resolution of 0.5 μm**
2. Multi-contrast acquisition, enabling **Quantitative Phase™** and **Subresolution Darkfield™** information along with absorption contrast imaging
3. Optimization for **in-situ imaging** through system design and novel direct detection system
4. Advanced reconstruction algorithms

The following subsections will detail each advantage.

I.1 Industry-leading Resolution of 0.5 μm

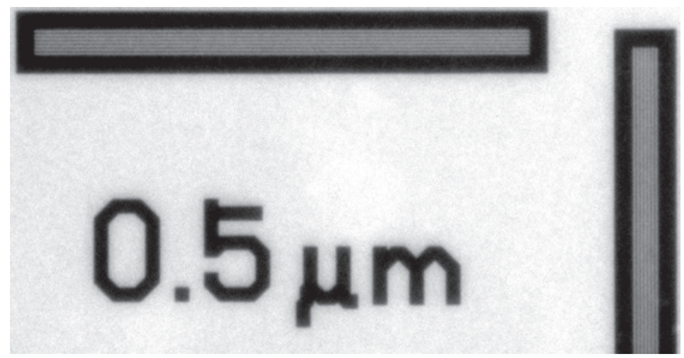


Figure 4: *Resolution standard (JIMA) imaged at 0.5 μm on PrismaXRM*

PrismaXRM offers down to 0.5μm resolution and, more importantly, ***maintains*** high resolution, even at large working distances, which are often required for practical sample sizes and planar samples. In contrast, most microCTs/XRMs are limited to ~1μm spatial resolution at best, and are even further limited (e.g. 5-10μm) at large working distances.

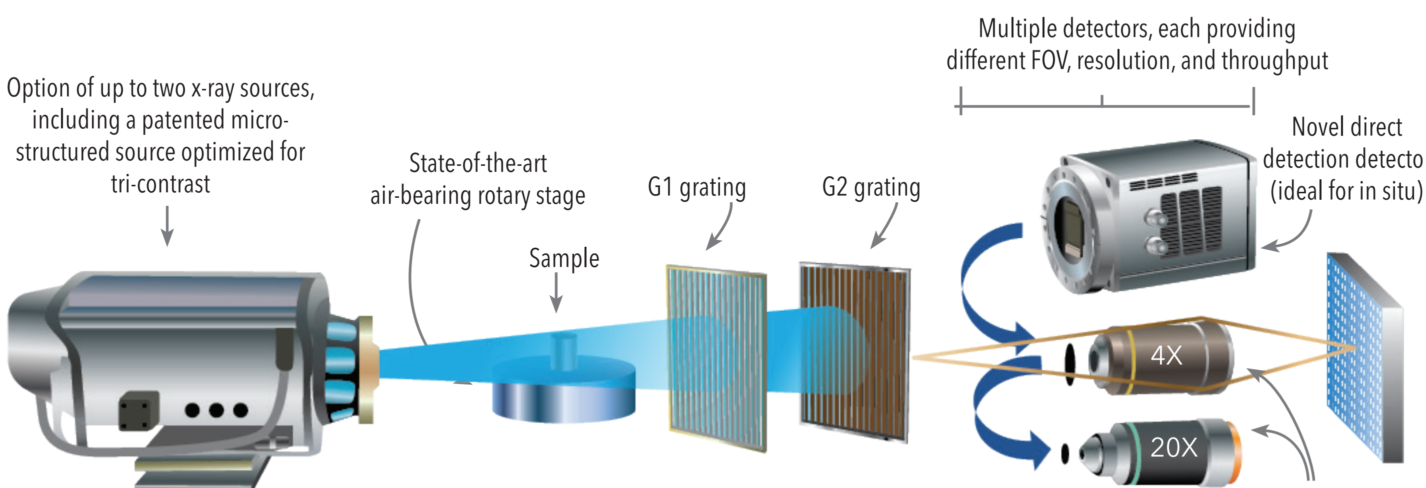


Figure 3: *Schematic of PrismaXRM system design shown in multi-contrast mode: an x-ray source (option of up to two in the system) illuminates a sample and a series of gratings in tri-contrast mode to acquire absorption, phase, and darkfield simultaneously. The gratings can be retracted for absorption-only mode imaging. Several detector options are included, including a novel direct detection camera and several optical magnification based x-ray detectors.*

The excellent resolution performance of the PrismaXRM is achieved using a high powered source with a nanofocus spot size in combination with a high resolution detector system that provides down to submicron pixel sizes.

I.2 Novel Multi-contrast Imaging

To enable simultaneous acquisition of multiple contrasts, the PrismaXRM incorporates an exciting new laboratory approach recently developed called grating-based interferometry (GBI). GBI systems have largely been pursued by research groups for medical imaging. Sigray has developed a high resolution, high throughput approach to GBI specifically for **x-ray microscopy**.

How does PrismaXRM acquire multiple contrasts? GBI works by creating an interference pattern near the detector. As shown in Fig. 5, the interference pattern changes based on the absorption, phase shifts, and scattering encountered by x-rays passing through the sample. PrismaXRM enables separation and measurement of these changes.

Creating the interference pattern required for GBI can be accomplished by using PrismaXRM's high resolution nanofocus x-ray source or its second patented x-ray source, which was designed specifically for GBI. The source has a microstructured target that produces structured illumination, resulting in an interference pattern when illuminating a downstream grating via the self imaging effect.

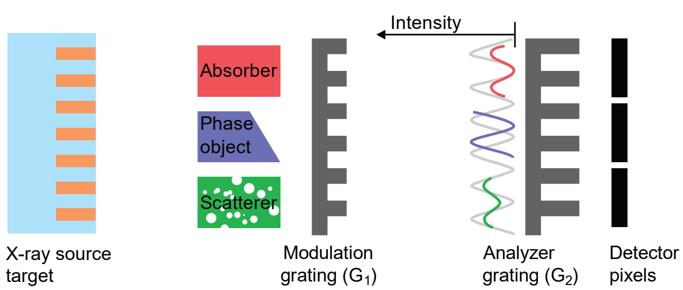


***Figure 5:** Patterned illumination from the X-ray source interacts with the sample and a modulation grating (G1). Absorption, phase, and scattering signals are then sampled by an analyzer grating (G2) onto the detector.*

The value of using Sigray's patented microstructured source is that it more than doubles the throughput [1] compared to the major alternative method of achieving GBI using an absorption grating (typically called "G0") placed in front of an extended laboratory source. The Sigray PrismaXRM approach also ensures a substantially wider field of view (FOV) and enables multi-contrast acquisition at x-ray energies above 40 keV, which is needed for penetrating through most non-biological samples.

The ultimate benefit of PrismaXRM's GBI is that it acquires not only conventional absorption contrast imaging, but simultaneously acquires two additional contrasts: Quantitative Phase™ and Subresolution Darkfield™.

I.2A Quantitative Phase™: What is it? Why is it important?

Quantitative Phase™ is a type of phase contrast that is far more powerful and sensitive than the more well-known Propagation Phase Contrast (PPC). PPC is the second derivative of phase and can be seen on standard x-ray microscopes just by placing the sample far from the source and detector. In fact, PPC is also achievable on the PrismaXRM in absorption contrast mode.

However, PPC is largely been considered not useful (and even sometimes detrimental) for several reasons:

1. PPC has very **slow throughput** due to the requirement that the sample must be placed far enough from the x-ray source to generate spatial coherence. Because flux falls off with the square of the distance, flux becomes very low.
2. PPC is limited to low **x-ray energies**
3. It is difficult to separate from absorption information, which makes the data **difficult to analyze** quantitatively
4. It is typically not practical to quantify, requiring multiple (2+) low throughput tomographies at different distances. PPC is thus usually only able to qualitatively enhance edges

Many users familiar with PPC are not aware that other forms of phase contrast exist. Unlike PPC, PrismaXRM's Quantitative Phase™ is proportional to the first derivative of the phase and is directly integrable (quantifiable). **Quantitative Phase™ eliminates the problems of PPC**, enabling: higher throughput, operation at higher energy, and quantification of electron density in samples. Its high sensitivity also reveals small density differences that are not seen in absorption contrast (Fig. 6).

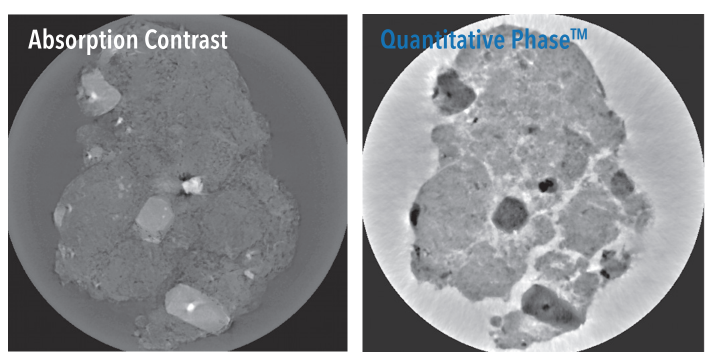


***Figure 6:** Absorption-based image (left) and phase retrieved image (right) of soil. Density information encoded in Quantitative Phase™ cannot be seen in absorption-based imaging.*

Quantitative Phase™ is a breakthrough for not only low atomic number (Z) samples such as unstained biological and polymer samples, but is also powerful for geological and ceramic material samples. These latter samples are typically complex, having different phases that are indistinguishable with absorption contrast alone.

I.2B Subresolution Darkfield™: What is it? Why is it important?

The other novel contrast accessible exclusively in PrismaXRM's multicontrast mode is Subresolution Darkfield™, which provides information that can not be resolved using absorption contrast. Darkfield has recently become a major topic of interest because of its unique ability to rapidly locate defects (cracks, delamination, and voids), determine fiber orientation and other anisotropies, and map nanoparticle distributions.

Subresolution Darkfield™ measures x-ray scatter and excels at finding unseen features (e.g. nanopores, cracks, nanoparticles) that are below the resolution of the system and therefore cannot be detected in absorption contrast. In fact, typically the smaller the feature, the larger the scattering angle, making it easier to detect. Darkfield signal also depends on the relative orientation of the structure, and the signal can be used to quickly (within minutes) measure orientation of fibers in a sample without needing to resolve the individual features.

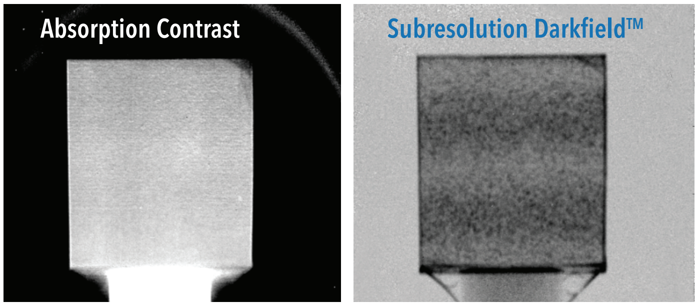


Figure 7: *Subresolution Darkfield™ shows orientation of this carbon fiber reinforced polymer (CFRP) sample is along the Z axis (into and out the page). These fibers cannot be resolved using absorption contrast.*

I.3 Optimization for In-situ Imaging

The ability to image samples in situ under environmental conditions (temperature, mechanical stress, fluid flow, etc.) is a key advantage of x-ray imaging systems. Sigray has optimized PrismaXRM for state-of-the-art in situ imaging through the selection of multiple detectors (see Fig. 3), each offering a different advantage for in-situ performance:

- **High throughput**: PrismaXRM offers a new breakthrough direct detection detector with significantly higher modulation transfer function (MTF) than flat panels. Moreover, this particular detector was designed for high efficiency detection of x-rays over 60 keV, which is advantageous for samples in large in-situ rigs.
- **Highest resolution**: Multiple optical magnification-based detectors provide variable magnifications (e.g. 4X, 20X) at high resolution. Similar to objective lenses on a visible light microscope, these lenses enable "zooming in" and "zooming out" on features of interest. Such detectors are particularly advantageous for advanced in situ imaging because they provide very small pixel sizes, enabling submicron resolution imaging even when the sample is placed in an in situ cell.

I.4 Advanced Reconstruction Algorithms

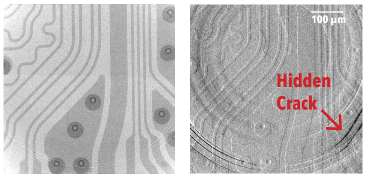
Sigray's reconstruction engine incorporates the most recent and advanced learning algorithms available. The post-processing suite features industry-leading data optimization & noise suppression techniques, available within a GPU-accelerated reconstruction environment. Users can take advantage of built-in reconstruction workflows or customize the processing pipeline via interactive, user-friendly parameter adjustments. Industry-standard image processing environments are also provided, featuring AI-assisted image segmentation modules, trainable machine-learning data processing workflows, and a state-of-the-art 3D-4D visualization engine.

II. Summary and Example Applications

Sigray's team designed PrismaXRM to break through the limits of 3D x-ray microscopy to enable new insights that were previously inaccessible using even the highest performance systems. PrismaXRM combines advances in x-ray source, x-ray detector, and acquisition and analysis to provide the highest imaging resolution (0.5 um) available, in addition to new multi-contrast imaging.

A few of the exciting examples of PrismaXRM's applications, spanning from academic materials and biological research to industrial semiconductor and pharmaceutical research, include:

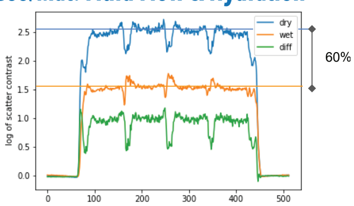
Semiconductor: Failure Analysis



Absorption   Quantitative Phase™

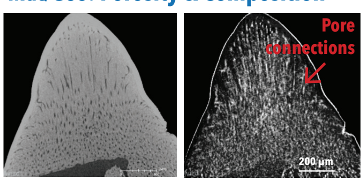
Challenging defects that were previously invisible for x-ray microscopy are now visible using the new contrast modalities on PrismaXRM. These include cracks (both in metal and silicon), voids and underfill, and delamination. See referenced publications for more detail [2,3].

Geo/Mat: Fluid Flow & Hydration



For conventional microCT, fluids often need to be doped to be visible. Subresolution Darkfield™ provides a clear signal difference between hydrated and unhydrated porous structures without contrast agents. Shown on the left is the quantitative change in darkfield signal across a catalyst that was dry and then hydrated.

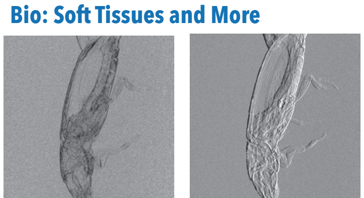
Mat/Geo: Porosity & Composition



Absorption   Subresolution Darkfield™

Multi-contrast provides rich information on porosity and composition, which are critically important in materials and geological studies. As shown on the left, Subresolution Darkfield™ reveals pore connections below the resolution of absorption contrast. Further, Quantitative Phase™ provides quantitative electron density information that complements absorption's atomic number information to provide complete compositional/mineralogical information as illustrated in Fig. 6.

Bio: Soft Tissues and More



Absorption   Quantitative Phase™

Quantitative Phase™ is particularly powerful for biological samples because it is based on density changes in a material, providing up to three orders of magnitude (1000X) stronger contrast than absorption. Features in plants and soft tissue can be seen without requiring contrast agents.

Discoveries made possible by multi-contrast imaging are just beginning, and the PrismaXRM is expected to be integral in pioneering new research approaches and for establishing future high impact publications. See what you've been missing with a complimentary demonstration of your samples on the Sigray PrismaXRM.

1. G Zan, DJ Vine, RI Spink, W Yun, Q Wang, G Wang. "Design optimization of a periodic microstructured array anode for hard x-ray grating interferometry," Physics in medicine & Biology Vol. 64:14 (2019).
2. SH Lau, et al. "Addressing Failure Analysis challenges in advanced packages and MEMS using a novel Phase and Darkfield X-ray imaging system," ISTFA 51598 2020.
3. SH Lau, et al. "Defect characterization of advanced packages using novel phase and dark field x-ray imaging," Electronic Device Failure Analysis Vol. 22 No. 3 (2020): 18-25.

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