Making the Invisible Visible through Timepix Technology: putting science on the market

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Amsterdam Scientific Instruments is an Amsterdam based high-tech spin-out from a large Dutch national research institute. The company intends to become a global player in the market of radiation detectors for the scientific and industrial market. The team consists of members who have worked at several research institutes regarding X-rays and gained larged amounts of knowlegde about this field. The spin-out produces, delivers and further develops state-of-the-art X-ray imaging cameras for the high-end segment of the scientific market. In this market they are used in photon science and neutron imaging. In photon science they are used for X-ray imaging, synchrotrons and/or "Free Electron Lasers" (FEL). Especially hybrid pixel-detectors with semiconducting sensors, because they have proven to be of much more general use than for high-energy physics experiments only. The cameras are suitable for X-rays, neutrons, ions and electrons. They are produced, delivered and further developed by the company are based on the Medipix/Timepix chips. The innovations that the company has put forward makes it possible to have cameras with a larger detector area and data read out speed. In addition, the high resolution of the detectors puts foreward detailed images.

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1. Introduction

ASI Holding is made up of two innovative technology companies, Amsterdam Scientific Instruments (ASI) and Omics2Image. The ground-breaking technologies used in both companies' solutions were developed at Nikhef, the National Institute for Subatomic Physics, and AMOLF, one of the research laboratories of the Foundation for Fundamental Research on Matter. Our imaging solutions are based on a technology platform with "smart" pixels, the Timepix technology, and proprietary hardware and software, that allow for a new approach to electron tomography, mass spectrometry imaging, color X-ray images, and neutron radiography. The detectors are offered as components for OEM partners that can integrate it into their end products and directly to consumers. What does this mean for industries such as life sciences, chemical, forensics, clean-tech, manufacturing, and agrofoods? The technology allows our customers to open up a whole range of new applications, discover more, and save time and money.

For more than a century, conventional imaging systems have been producing images with levels of grey-scale as the only indication of a sample's internal structure. ASI technology removes this limit using a new type of readout chip (Timepix) developed by a CERN led collaboration. This Timepix chip allows for a new approach towards "color" X-ray images and a molecular camera. It makes it possible to look at cells in a 3D view, or look at cells layer by layer. Cutting edge imaging solutions are enabled through the combination of this chip with proprietary readout electronics and sensor technology. In addition, ASI has developed application specific software, to control customers' experiments, data collection, post-processing and data analysis.

In short, ASI offers imaging solutions that are being used in ways that have never been possible before, ranging from:

- Achieving improved quality control, such as in polymer film testing
- Testing a painting to determine its authenticity
- Testing human cells to see whether they will respond to chemotherapy
- Performing high resolution hair analysis to test for drug use
- Discovering new morphologies of crystals to create customized medicine
- Achieving very early detection of cancer cells
- Performing non-destructive testing of new composite materials in aerospace
- Developing and testing nanomaterial packaging in the food industry

ASI's technology can turn testing tools into discovery tools by enabling the user to visualize whatever she has not been able to visualize before. Examples include:

- Molecular structures
- Nanocrystals
- micro fractures
- Color in images

In addition, existing mass spectrometry products do not provide any way for the user to see the image they want to capture before initiating the experiment. This means the user spends valuable lab time "tuning" the instrument to get the approximate result he is looking for. With ASI's technologies, you are able to actually have a visual of the molecules before the experiment is initiated, reducing preparation time. This also means that companies and research institutions save time and money on training people, since this makes mass spectrometers easier to use.

To sum up some technical benifits of the Timepix technology:

Electron Microscopy

- Allows use of EM for studying smaller crystals

From 100 um to 1 um

- Gives access to full 3D structural information at atomic resolution

Higher sensitivity allows for dose reduction, causing less radiation damage to sample
Large angle coverage in minutes

- Saves money

Low-cost alternative to multi-billion Euro synchrotrons XFELs
Substantially reduced (x1/1000) number of samples required

Mass spectrometry

- Reveals the finest structures of biological samples in 3D

Resolution < 0,5 um

- Dramatically increases sample throughput

From 2 days to < 5 min
Over ¼ million spectra per image

- Accelerates development of personalized medicines.

1000x more sensitive

ASI's mission is to enable accelerated innovation for our customers by pushing the boundaries of technology for scientific applications. It is our goal to create customer value by developing, building, and delivering the best and most reliable imaging solutions, in a wide range of industries. Everything we create delivers on our vision to make the invisible visible.

2. Technology

The products that ASI offers are Timepix hybrid detectors. They use Timepix chips which have been development in the Medipix collaboration. The technology behind the Timepix is that the sensor chip is bump-bonded, which is a method for interconnecting electric components, to the readout chip. Each pixel contains its own electronics and therefore can use three different measurement modes. This technology has been put into two types of cameras, namely with a pixel array of 512x512 or 256x256, sensitive area 1.4x1.4 cm2 or 2.8x2.8 cm2. Together with certain software, it is possible to read out the large amounts of data that comes out from cameras. The company strives to build large area cameras (4.2Mpixels, 12x12 cm2) that can

handle the high data rates involved in experiments with current and future light sources. The cameras are stirving to reach 1k frames per second, currently the rate is 120 frames per second.

The cameras that ASI has developed can be used for precise spatially and energy resolved detection of X-rays, ions, electrons and neutrons. Using the cameras in X-ray imaging makes them an excellent tool for the bright X-ray sources. When using a bare Timepix chip in combination with a micro-channel-plate it is an ideal tool for Mass Spectrometric Imaging (MSI). By covering the sensor with a material (e.g. 6LiF), neutrons will be converted into the radiation that is detectable by the silicon in the camera. In the current state the cameras are sold to the high-end scientific market. This in order to establish a position as a high-tech spin-out that is capable to build and deliver state-of-the-art X-ray, neutron, electron and ion cameras to new markets. The technology that is used in the camera is unique because of the three measurement modes that can be used. These modes are event counting, "time-over-threshold" and time-of-arrival.

Other technologies used for X-ray imaging are XPAD and PILATUS detectors. When comparing the Pilatus cameras to the camera that ASI offers, the difference lies in the smaller pixel area which results in better spatial resolution. In addition, the cameras using the Timepix chips offer time-resolved and energy-resolved measurements opening additional applications unavailable with the Pilatus detector. When comparing the XPAD and Timepix cameras, it can be concluded that the XPAD allow making larger cameras, but the Timepix has a much better spatial resolution.

The USP of the imaging cameras is that they use the timepix chip. This chip makes it possible to have three measurement modes:

- Counting mode
- Time-over-threshold (TOT)
- Time-of-arrival

These modes can be implemented independenttly in each pixel. An external reference clock is used to generate the clock in each pixel that increments the counter depending in the selected operation mode with a maximum frequency of 100 MHz.

3. Market Applications

ASI's imaging solutions can be used in a vast array of market applications, and we are hearing about new applications every day from our customers. Below are a few examples of how scientists in a wide range of industries are applying ASI's technology to achieve unprecedented results.

Lifesciences/Healthcare
Our noise-free X-ray detectors are so sensitive that they can see signals most other detectors cannot. This means that technicians can obtain excellent image quality with less radiation. As this enables them to lower the effective radiation exposure, it is much safer for both staff and

patient. In addition, our systems provide unparalleled image quality, and our detectors obtain spectral/structural information (on top of intensity/anatomical information), which enables "color" inclusion in CT images, and subsequently assists technicians to determine what an object is actually made of. The combination of both features allows technicians to see subtle differences that may have been left unrevealed in the past. These subtleties can be vital to the care physicians can provide their patients. These are just a couple of examples of how ASI's imaging solutions are expanding the possibilities for truly personalized medicine.

Manufacturing

For the Manufacturing industry, many gains can be made, particularly in the area of Quality Control. Examples include weld inspection for the piping industry, checking the structural integrity of composite materials in industries such as aerospace, or inspection of packaged food and pharmaceutical products in regards to glass, metal, and other physical contaminants. This means that manufacturers can achieve higher throughput targets by faster and more reliable quality control of their manufacturing process, increase profitability by avoiding unnecessary and costly product recalls, and improve the quality of end products that may be affected by X-ray radiation.

Chemicals

ASI's imaging solutions have many applications in the chemical and petrochemical industries. The technology can be used for the analysis of polymer films, to determine how homogeneous the surfaces are, and allow chemists to diagnose process problems as they're happening. In the petrochemical industry, the technology can be used to optimize a detergent mixture to get oil out of the ground using the least amount of materials to obtain a better, more sustainable result. In all cases, this radically improves the end result while saving time and money.

4. ASI: We Make the Invisible Visible

ASI's mission is to enable accelerated innovation for our customers by pushing the boundaries of technology for scientific applications. It is our goal to create customer value by developing, building, and delivering the best and most reliable imaging solutions, in a wide range of industries. Everything we create delivers on our vision to make the invisible visible.