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History and future of radiation imaging with single quantum processing pixel detectors

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ABSTRACT

This introductory article treats aspects of the evolution of early semiconductor detectors towards modern radiation imaging instruments, now with millions of signal processing cells, exploiting the potential of silicon nanotechnology. The Medipix and Timepix assemblies are among the prime movers in this evolution. Imaging the impacts in the detecting matrix from the individual ionizing particles and photons can be used to study these elementary quanta themselves, or allows one to visualize various characteristics of objects under irradiation. X-ray imaging is probably the most-used modality of the latter, and the new imagers can process each single incident X–photon to obtain an image with additional information about the structure and composition of the object. The atomic distribution can be imaged, taking advantage of the energy-specific X-ray absorption. A myriad of other applications is appearing, as reported in the special issue of this journal. As an example, in molecular spectroscopy, the sub-nanosecond timing in each pixel can deliver in real-time the mapping of the molecular composition of a specimen by time-of-flight for single molecules, a revolution compared with classical gel electrophoresis. References and some personal impressions are provided to illuminate radiation detection and imaging over more than 50 years. Extrapolations and wild guesses for future developments conclude the article.

1. Radiation imaging

Particle detectors detect particles, and the original intention in 1988 was that the micropattern detectors would recognize the type of incident particle by detecting their characteristic microscopic patterns of energy deposition created in the matrix of active pixels (Heijne et al., 1988). Now these devices are better known as ‘pixel detectors’, in analogy to ‘microstrip detectors’, and which of course do not detect pixels or strips, but ionizing quanta such as electrons, protons or photons. Electronic processing of the signals induced in the segmented sensor material by single quanta of radiation results in a true 2-dimensional (2D) image for pixel detectors, or a projected, 1-dimensional (1D) mapping of the positions of the induced signals for a single-sided array of strips. The revolutionary idea of the pixel detector is to implement the complete, classical nuclear detection chain, including front-end signal processing, digitization and nanosecond timing on a microscopic silicon area, that matches the segmentation of the attached sensor, and then integrate ten-thousand or even a million of these cells into one instrument. This becomes possible by exploiting the incredible developments in semiconductor silicon technology. The images induced by radiation quanta with these parallel, segmented sensing elements can be recorded in a few tens of nanoseconds. These detectors nicely illustrate the impact of microelectronics on detection, which Pierre Jarron and the author predicted in their 1984 article (Heijne and Jarron, 1984). Already in the 1950’s, nanosecond timing for separate quanta was possible with single sensors, and also full frame imaging was possible, but only by integrating incident light and with slow media such as photo-sensitive film. Now, pixel detectors combine these features in one instrument. The Medipix collaborations have a sustained activity in this field since the mid-1990’s, and while they have no claim to be the only game in town, the Medipix and Timepix imaging devices with their associated readout systems make a significant impact in ever more applications, to be described by other authors in this issue. This introductory article illustrates the impact of semiconductors, silicon and ASICs in particular, on imaging of elementary particles and photons. The amazing properties of silicon are emphasized, and comparisons are made with earlier instruments. One should expect more progress to come, because radiation imaging has by far not incorporated recent nanotechnologies, the cutting edge for today’s products from the chip industry.

Imaging ***of*** radiation quanta, first of all, aims at understanding the radiation itself. Photographic plates quite by accident led to the discovery of X-rays by Wilhelm C. Röntgen in 1895 and of radioactivity by

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A. Henri Becquerel in 1896. Nuclear emulsions with silver-chloride or -bromide grains then, over several decades, enabled numerous discoveries. Nearly a century later, thanks to its 3-dimensional (3D) recording with sub-μm precision, emulsion still was used for measuring particle decays with ∼mm pathlengths involving charm and beauty quarks, illustrated in Fig. 1a (Adamovich et al., 1981). For elementary particle research the dimensions of 3D imaging detectors have grown with the increase of energy needed to create massive quanta such as the Higgs boson. These have to be reconstructed from the tracks of their decay products in the imagers. Instruments registering transient electronic signals become imperative instead of recording in emulsion, or other low-response-rate systems such as the once successful 3D bubble chamber. Dense particle flux and high interaction rates, e.g. 40 MHz at the Large Hadron Collider (LHC), are imposed by the low probability of the interesting phenomena. Silicon pixel detectors have been installed as innermost particle tracking instrument. They record 3D coordinates of all ionizing products coming from the interactions, and allow their detailed reconstruction, as illustrated for an interaction in ATLAS, Fig. 1b. Here is not the place to discuss particulars of the LHC detectors, but it should be mentioned that the 3D reconstructions at LHC are based on rather a sparse set of sensing points, contrary to the emulsions or bubble chamber pictures. The imaging pixel detectors introduced in this article might fill the gap between very sparse recording and full-volume imaging. A virtually undivided, sensitive volume with microscopic 3D resolution is eminently sensitive for imaging of relatively low energy processes, of particle decays with ps to fs lifetimes and for position measurement with submicron precision.

For the radiation environments on earth, in space or inside equipment, a better characterization in dosimetry can be achieved by imaging of the individual incident quanta in the radiation. For example, alpha particles or heavy ions can be recognized and these contribute more biological damage than electrons or photons.

The other, more practical interest is imaging ***with*** radiation, for the study of any sort of object, in materials science, in art or in medical treatment. In this special issue many such imaging applications will be reviewed. Physics research over the last centuries not only has widened the range of electromagnetic wavelengths that we can exploit, far above and below the visible frequencies of 430–770 THz, also it has enabled imaging with electron microscopes and other accelerators for imaging with protons, neutrons and ions. Not long ago, most of the X-ray practice still was based on the traditional and versatile photographic plates, but since ∼1990 a variety of electronic imaging devices have come to the market. Here the distinction between direct and indirect (via visible light) electronic imaging has to be kept in mind, as well as the difference between integrating and quantum/pulse-processing imaging methods. Fully parallel signal processing is a major innovation for radiation imaging. Without being mentioned explicitly, this was already demonstrated in the first work on the silicon microstrip detector (Heijne et al., 1980), where all analog signals were processed over parallel channels until after digitization. Such multi-channel pulse-processing was earlier used in the Multi-Wire-Proportional-Chamber (MWPC) with ionization in a suitable gas mixture. For MWPC delay-line readout was often considered superior, because it would reduce the number of external connections, but in the highly segmented silicon matrix devices, 1D microstrip or 2D pixel detectors, and with thousands of simultaneously incident particles, the parallel approach is the preferable solution. Implementation of millions of parallel sensing channels in a compact way, moreover, has become a realistic option, since silicon integrated circuit technology allows such a level of complexity at affordable expense. The silicon technology now opens the way for microscopic imaging based on detection of individual energetic quanta that compose the incident radiation. The most simple approach is photon counting in X-ray imaging, but much more powerful methods can be implemented by adding intelligent processing of the single quanta. For example, photons can be weighted according to their individual energy, so that the indiscriminate and excessive ‘darkening’ by the all-penetrating, high-energy quanta is reduced. For ionizing particles, their directions of movement might be determined in the imager, so that those can be excluded which do not come from the object under study. Imaging is being revolutionized, just as nanoelectronics on the whole is changing our society and our earth, hopefully for the better.

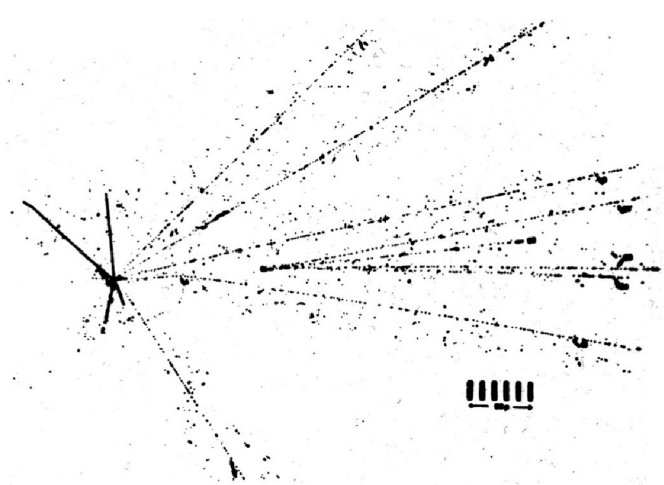

Fig. 1a. Interaction in emulsion by photon incident from left, in the CERN-Omega experiment WA58. Scale of 50 μm is indicated. Secondary decay vertices can be recognized. The large number of ionized grains results in high fidelity. 36 L of emulsion was exposed and interactions located with help of a silicon microstrip telescope and wirechambers in the spectrometer (Adamovich et al., 1981). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

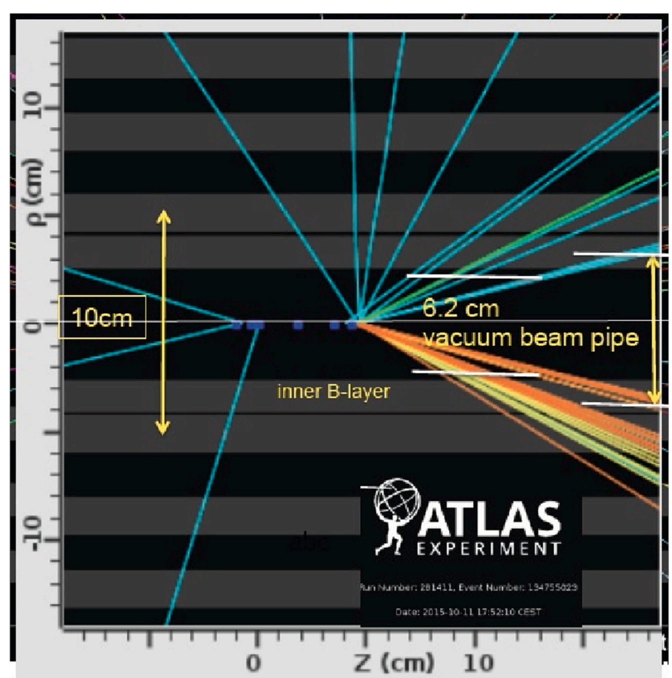

Fig. 1b. Interaction between two colliding protons in the LHC experiment ATLAS. The higher energy elongates the decay lengths of the secondary particles. The left vertical arrow is 10 cm. The gray bands indicate the positions of the 4 pixel layers surrounding the crossing point of the beams [CERN-ATLAS].

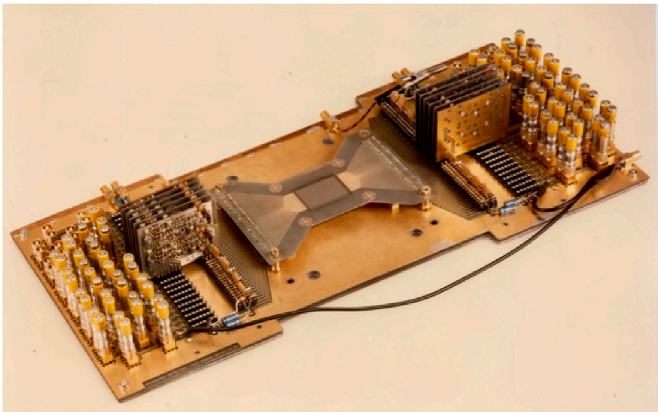

Fig. 2a. The first Si microstrip detector mounted on a readout board for testing at the CERN SPS H6 beam (Heijne et al., 1980).

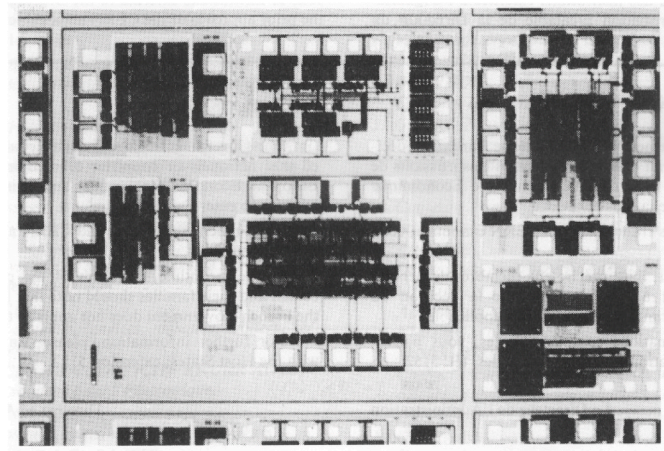

Fig. 2b. Test chip in 3 µm CMOS technology, featuring several circuits designed by 8 CERN engineers (CERN Weekly Bulletin, 1986).

2. Semiconductors change nuclear and particle physics, and the world at large

Semiconductor physics and devices gained interest, once reproducible growing of single crystals of germanium Ge and silicon Si became feasible, during the 1950's in different research labs such as Bell, General Electric Schenectady and Philips Eindhoven. Soon, crystals became available commercially from Montecatini and Wacker in Europe, and from Monsanto in the USA. Until then, semiconductor materials research and device development had been somewhat of a backwater in physics. State-of-the-art was extensively documented in the 1959 handbook 'Semiconductors' by Smith (1959), but with little emphasis on silicon. Following the explosive evolution of Si technology, now in 2017 the worldwide sales of Si integrated circuits amount to 420G$, and approach the sales of grains and rice for food, which was worth 651G$ in 2016. Today, books about silicon technology and chip design abound. Amazingly, in spite of the overwhelming impact of silicon on society, education programs in schools still do not provide the young people with much of the basic knowledge about semiconductor characteristics.[1] Silicon solar cells catch photons for electricity generation, acting in some way as radiation detectors, but silicon devices could be more useful in directing energy flows for manufacturing, heating or transportation.

In the context of the wide-ranging, post-war research efforts, the first semiconductor devices immediately found applications in nuclear experiments. Energy spectroscopy of nuclear processes became easier with the compact germanium detector from 1950 onward, even if this has to be operated at liquid nitrogen temperature of 77 K. Silicon detectors were introduced by 1960 and soon became the standard detection element in the scanning electron microscope, and in many other applications involving radiation. Companies in the USA as well as in Europe started manufacturing and marketing these specialized instruments. Some of this history was reported by the author, in a review about the Low Countries (Heijne, 2003), and here are recalled the first operating semiconductor particle detector, AgCl at liquid air temperature, conceived by Pieter van Heerden (Heerden, 1950) in Utrecht 1943 (Heerden, 1945), and the first large-scale system using 'checkerboard' detectors, front/back crossed electrodes on silicon wafers, also operated in the Netherlands, from 1965 onward at the IKO nuclear research institute in Amsterdam (Hofker et al., 1966; Koerts et al., 1971). However, the world of detectors for invisible 'nuclear' radiation soon became detached from mainstream semiconductor electronics, and for quite some time the opportunities for integration of functions were hardly recognized.

The main condition needed to improve crystal growing, manufacturing and semiconductor device reproducibility is the clean processing environment. Now this may seem trivial, but it was not straightforward to achieve. Today, silicon device processing proceeds in disciplined and strictly controlled enclosures, with high-purity chemicals and without direct human contact, so that very low contamination levels can be achieved. The early germanium and silicon detectors were manufactured on traditional chemical benches, and yet it was found that good quality detectors could be made with the gold-on-high-resistivity-n-type silicon 'surface barrier' technology. For two decades this was 'state-of-art', while diodes made with the diffusion technology (Keil and Lindner, 1972) or with ion implantation (Zandveld, 1976) at that time usually presented problems such as high dark current or high noise,[2] most likely related to impurity diffusion during the high-temperature steps, which are avoided in the surface barrier metal evaporation.

Change came only when Josef Kemmer by 1980 improved the dark current and the noise of the diodes by applying more recent, clean industrial conditions, for the silicon oxidation and the ion implantation (Kemmer, 1980). When Kemmer's approach was subsequently adopted by a few European and Japanese suppliers, much better quality detectors became available. In this context, the major contributions in these early days by Paul Burger, Colin Wilburn and Keio Yamamoto ought to be mentioned. Very precise sensor segmentation became possible by using lithography of the silicon-oxide layer (Kemmer et al., 1982) instead of the metal contact evaporation through masks, as was used for the checker board detectors (Koerts et al., 1971) and the first microstrip detectors, Fig. 2a (Heijne et al., 1980). More details on this 1980 'detector revolution' can be found in another review (Heijne, 2008). The oxide-passivated, ion-implanted silicon microstrip detectors soon were widely adopted for particle physics experiments and multi-layer tracking and vertexing telescopes were installed, also in space-based instruments.

For the detector team in the EF Division at CERN it was clear that in the future proton colliders, then under discussion: ISABELLE, the SSC,

[1] As illustration, physics teachers should tell their class that diode thermal leakage current reduces the efficiency of semiconductor photovoltaic (PV) solar cells by 20%–40% at higher temperatures, such as 50°C for Si, and they would work better in the cold than in a hot sunny desert. Anyway, solar PV cells at best convert ~ one-fifth of the incoming solar energy in electricity and using the heat might be better. Still, PV is not bad in comparison with the energy-efficiency of agricultural production for electricity generation or transportation with biofuels, which is less than 2%.

[2] Zandveld reports in (Zandveld, 1976) a diode reverse current of 1 nA/cm2 for the implanted diodes with beveled edge, but these were not used for their BOL project due to large 1/f noise (private communication).

the Eloisatron and the LHC, neither the microstrip detectors nor the serial Charge Coupled Devices (CCD, see next chapter 3) would be capable of dealing with the high multiplicities and high rates. With a fairly thin silicon layer and small sensor cells an adequate noise performance might be obtained, but in the early 80's the usual electronics with discrete components could not be made equally small. We would need to learn designing integrated circuits ourselves, and this would take time. Contacts with the Flemish Inter-University Micro Electronics Center (IMEC) in Leuven eventually led in 1986 to a training course for 8 CERN electronics engineers. A demonstration chip in a 3 μm CMOS n-well technology, Fig. 2b, was the practical result of this exercise (CERN Weekly Bulletin, 1986). Quite to the surprise of many colleagues, all the circuits on this test chip performed according to the plans. Soon afterwards, the chip design effort at CERN was strengthened by support in the framework of the LAA detector R&D project. Five microelectronics designers joined the small team, which until then was just Pierre Jarron, two CERN Fellows, and the author. Our design activity first focussed on AMPLEX, a 16-channel readout chip (Beuville et al., 1990) for a pad detector that was going to be used in the inner silicon tracker in the UA2 experiment. By chance, in 1988 this would turn out to become the first integrated circuit used in a collider experiment, with also the largest silicon detector to date: UA2 installed two layers with a total area of 1.2 m^2 of Si sensors (Ansari et al., 1989). The pads in these detectors were fairly large, with capacitance of 100 pF for the outer and 15 pF for the inner layer, but noise was low enough to record the signals of minimum ionizing particles, and in particular the electrons that came directly from the primary interaction. This helped in the physics analysis to suppress backgrounds from conversion electrons, generated in the material of the original tracker using scintillating fibers. In a way, this two-layer UA2 silicon array was the earliest pixelated tracker, although using large pads. One innovation, hardly mentioned at the time, was the stacking of the chips and boards for the readout directly on top of the sensors, both taking an equal surface area, and all connections on the outer ends of the cylindrical assemblies. Afterwards, this arrangement has become standard for the tracker detectors in particle colliders, and really is a consequence of using miniaturized integrated circuit technology, which reduces the size of the electronics by a large factor.

Two parallel approaches to introduce microelectronics for the Si microstrips in physics experiments had started earlier, one in a collaboration with Stanford University and SLAC[3] and the other by a team in the Max Planck Institute (MPI) in Munich, with W. Buttler from the Fraunhofer Institut Duisburg, and Franco Manfredi from the university of Pavia. This led to respectively the Microplex circuit (Walker et al., 1984), and the CAMEX CMOS chip (Buttler et al., 1988), which were specifically designed for small capacitance microstrip detectors, and intended for the experiments MarkII at SLAC (Adolphsen et al., 1988), for DELPHI and for ALEPH at the Large Electron-Positron (LEP) collider at CERN. The SLAC Microplex circuit was fabricated with the Stanford 5 μm n-MOS technology. Quite soon, a team at the Rutherford Appleton Laboratory (RAL) followed up with an improved, low power version, using a 3 μm CMOS technology, which then was actually installed in the silicon trackers of DELPHI and OPAL (Stanton, 1989; Allport et al., 1988). These chips used switched-capacitor feedback in the front-end amplifier, contrary to the continuous feedback loop in AMPLEX, for which Jarron exploited the high resistance of a long transistor. One advantage of the latter approach is inherent compensation for increasing dark current of the silicon diode detector element, introduced by the radiation damage. In fact, also later for the pixel detectors, this leakage current compensation is always a critical aspect of the circuit design. An elegant and efficient solution was introduced in 1990 by François Krummenacher (1991).

It is not the intention to describe here all the following steps in the developments of detectors and electronics over the 1980–2000 period. This would quickly occupy many pages, and other reviews can be found, e.g. by Michal Turala (2005) or Daniela Bortoletto (2015). Nevertheless, some general points remain noteworthy, now that specifically designed chips have become a basic issue in particle physics experiments. Contrary to the situation in many other fields of microelectronics applications, the choice in the particle physics community has been to learn ourselves so much detail about technology and design, that we achieve to obtain satisfactory circuits for our own use. Gifted engineers or physicists try to grasp the desired functionality, they are trained in chip design and verification techniques, and then organize the chip submissions, in collaboration with organizations such as IMEC in Belgium or MOSIS in the USA. We then usually receive complete silicon wafers, and have learned to execute their testing, dicing, packaging and evaluation. All this has allowed the particle physics community to efficiently install quite innovative systems in the experiments, at an overall cost that is very competitive with what it might have been, if fully industrial and commercial procedures would have been chosen. Moreover, these circuits have been optimized for operation in the severe radiation environments of the Fermilab collider and LHC experiments over the last decades, by extensive study of the basic effects and by technology and circuit evaluations. Radiation tolerance will not be further touched upon in this introduction to radiation imaging, but obviously it is essential also in several applications beyond pure experimental physics.

3. Radiation imaging with pixel detectors

The development of pixelated detectors for single elementary particles followed soon after the introduction of Si microstrip detectors, along two distinct lines, which here are described briefly, as an introduction to the present pixelated detectors for imaging. From 1981 onward, ideas for true 2D particle trackers first centered on monolithic devices: CCD and later CMOS imagers. CCD were under development since 1969 as imagers for visible light. Then in 1988 the CERN team introduced the alternative, hybrid pixelated tracker devices in which the sensor matrix is connected pixel-by-pixel to a CMOS readout chip. Both approaches were investigated in the CERN R&D collaboration RD19, between 1988 and 1999, and some of this work is here described. Basic issues in both approaches will be briefly compared. Earlier articles have been published on historical aspects of the novel pixel radiation detector development. A review of the beginnings was written in 2000 by the author (Heijne, 2001), Pierre Delpierre described various aspects (Delpierre, 2014), a recent extensive review was published by Maurice Garcia-Sciveres and Norbert Wermes with emphasis on high rate particle physics experiments (Garcia-Sciveres and Wermes, 2018), and a handbook on pixel detectors was written by Rossi, Fischer, Rohe and Wermes (Rossi et al., 2006), who are active themselves in the development and operation of the ATLAS pixel detector.

Electronic devices consisting of a matrix of elements have widely been used for a long time, and for example in the first 'core' memories each element was just a fairly large magnetized ring on the crossing of two wires. In R&D for electronic delay lines and memories, around 1968 engineers at Philips as well as at Bell Laboratories designed arrays of Metal-Oxide-Semiconductor (MOS) capacitors, connected by switching bipolar transistors (Philips, Bucket Brigade Device BBD (Sangster and Teer, 1969)), respectively by MOS gates as in field-effect-transistor switches (Bell, Charge Coupled Device CCD (Smith, 1970)). Both teams were well aware that their matrix also was light-sensitive, and might be used to record images, e.g. in a TV camera or a 'picture phone'. Yet it took nearly three decades of development before affordable and successful cameras could be mass-produced, and this work was mostly undertaken in Japanese electronics companies. Starting from the year 2000 the use of silicon-based imagers for visible light really took off, and by 2015 the yearly production surpassed 4 billion units (Teranishi,

[3] The suggestion to work with the Stanford University Microelectronics Group was made to the author by prof. Simon Middelhoek in Delft, and implemented by Bernard Hyams of the CERN EP Division in collaboration with Sherwood Parker and J.Terry Walker in Stanford.

2018), with Sony, Panasonic and Samsung as major suppliers for consumer applications. This growth came about by the combination of several factors: the introduction of portable 'cell' phones with built-in photography, the interconnectivity provided by the World-Wide Web, and the incredible miniaturization of complex functions on silicon CMOS chips which is the basis for all of this. Mass-production of imagers for visible light, now predominantly using CMOS technologies instead of the CCD processing (more on this later), reduced the price per unit to the amazingly low average of 3.5 US$.

These imaging sensors for visible light are sensitive to ionizing particle radiation as well, and in 1981, when CCD just became available for scientific use, still at thousands of US$ per unit, Chris Damerell and colleagues carried out experiments in the CERN NA11 collaboration (Bailey et al., 1983) on their use as a detector for particle tracking and interaction vertexing. They installed several devices, one behind the other, as an extension to the Si microstrip telescope already in use. It became immediately obvious that a true 2D detector is largely superior to the combined projections of several 1D microstrip detectors in a multi-layer telescope arrangement, in spite of the rate limitation by the slow serial readout of the CCD matrix. In such a matrix detector the usual ambiguities from simultaneously incident particles are avoided, much higher particle density can be handled and fewer planes can be installed, leading to a desirable reduction of material thickness, while even better precision can be achieved. A successful CCD-based tracker has been operated later in the Stanford collider experiment SLD (Damerell et al., 1989).

When during the 1980's the Complementary Metal-Oxide-Silicon (CMOS) technology became mainstream, this was also used to develop imaging arrays as an alternative for the CCD technology. For quite some time, the CCD remained superior in performance, but from ~2000 the majority of silicon optical imagers are manufactured in 'adapted' CMOS technology and only a small percentage still as CCD. A major difference is the way of reading the image, because the CMOS pixels can be addressed in various ways by line connections that run over the sensitive matrix, while in the CCD the signals are sequentially shifted through the matrix, moving the signal charge from one sensor site to the next, and towards a single, or sometimes to several output nodes. Another difference is the presence of a few transistors in each CMOS pixel, which lends these chips the name 'active pixel sensor' (APS) (Fossum, 1997). Until recently, these imagers were a monolithic, single chip matrix with ever more cells, but with relatively simple unit structure.

In view of the planned Superconducting Super Collider (SSC) in Texas, teams in Berkeley and in Stanford initiated studies for 2D matrix imagers to be used for particle tracking, as described in (Heijne, 2001). Using the custom CMOS processing facilities at the Stanford University Center for Integrated Systems, Sherwood Parker and Walter Snoeys developed a monolithic tracking chip which they tested at Fermilab in winter 1991–2 (Snoeys et al., 1993). Monolithic radiation imagers based on CMOS were also studied in the RD19 framework at CERN, but soon it became clear that fully parallel processing of current-pulses in all pixels, and achieving MHz frame-rates on a single substrate is difficult. In particular, the combination of circuits and sensors is challenging due to cross-talk. RD19 made the choice to use Silicon-On-Insulator (SOI) technology, with the substrate wafer used as the sensor and the intermediate oxide and an extra-deep well for signal isolation. A comprehensive description of results was published in 1994 as PhD thesis by Franz X. Pengg (Pengg (1996). Unfortunately, technological problems prevented these devices in the end to operate as designed. At that time, it turned out to be relatively easier to obtain working instruments in the hybrid approach. Some years later, the development of monolithic detectors has been taken up again, in SOI by a group at KEK in Japan (Miyoshi et al., 2011), and by several other teams using commercial CMOS technologies adapted for visible light imaging applications, and these imagers now are called Monolithic Active Pixel Sensors (MAPS). A group at the Université de Strasbourg initiated MAPS developments with a series of designs, named MIMOSA (Deptuch et al., 2004). Then also a team at RAL produced prototypes (Turchetta et al., 2006), which found applications beyond particle physics, such as in electron microscopy. Later on, Fermilab and Polish groups worked together (Yarema et al, 2013), and these efforts resulted in continuous improvements in performance. Still, in particle physics experiments the rate capability remained limited by lack of parallelism, which is easier to implement in the readout circuits for hybrid pixel architectures. From 2000 onward, work on monolithic devices gained more interest. Besides the groups already mentioned, there is the INFN project VIPIX, especially the Perugia group, and the development of the new pixel detector system for the ALICE upgrade in 2021. The CMOS imagers continue to have promise for imaging of radiation beyond the visible, when parallelism can be introduced and rates can be increased by sophistication of the architecture and by using multiple, stacked chip layers, which will be further discussed in chapter 5.

In parallel with these efforts on monolithic radiation imaging matrix circuits, in the early 90's the core activity, in the CERN-LAA team and later in the RD19 collaboration, centered on hybridized devices, somewhat similar to those developed already in the 1970's for infrared imaging. One major difference was the use of a Si sensor, while for military, space and security applications the imaging layer usually consists of an infrared-sensitive compound semiconductor material, which is bonded onto the silicon readout chip with soft solder bumps, because of different thermal expansion coefficients. In those earlier applications, the readout chips often were traditional CCD imagers with adapted cell layout and fairly long signal charge integration on the capacitive elements. Now, for particle physics applications two silicon layers are connected together, which should be easier with regard to compliance of the bumping, as no difference in thermal expansion has to be taken into account. The most revolutionary difference of the new hybrid devices compared to the earlier imagers, however, would be the implementation of a full, classical nuclear pulse processing in each pixel, rather than a simpler charge integrating mechanism. Moreover, also additional circuits such as digitization, local memory and pattern recognition should be placed in or near the pixel matrix itself, and the name 'micropattern detector' was introduced, with intention to identify incoming quanta via their specific patterns of ionization in the highly segmented matrix (Heijne et al., 1988). This hybrid approach at first was met with scepticism, as too complex a technology. The chances for successful development were discussed with several technology specialists, during the first 'Workshop on silicon pixel detectors'[4] in May 1988 in Leuven (Heijne et al., 1989). By the end of 1988 a small pixel matrix had been designed by the CERN LAA team, together with the microelectronics group at the Lausanne EPFL and with support by the particle physics group at the ETHZ and the Swiss National Fund. This readout chip was manufactured in the 3 μm SACMOS technology of Faselec AG in Zurich, tested in the summer 1989 and results were planned to be reported at the 1989 IEEE Nuclear Science Symposium in San Francisco. However, the Loma Prieta earthquake on 17 October led to cancellation of the Symposium, and the report was submitted to Nuclear Instruments and Methods (Campbell et al., 1990). Measurements had been made with silicon sensors connected to a few pixels, by wirebonding and not yet by bumps, because the external connections on the edge of this chip prevented placement of a matching sensor matrix. Fig. 3a shows the microphoto of this first pixel readout matrix with single quantum processing, and the radiation measurements are illustrated in Fig. 3b.

Immediately afterwards, the design of a more practical matrix was undertaken, still in collaboration with the EPFL Electronics Laboratory. François Krummenacher implemented the already mentioned dark current compensation scheme (Krummenacher, 1991), while Michael

[4] These Proceedings (Heijne et al., 1989) contain the transcripts of the discussions after each presentation, recording opinions and realities of that time. Unfortunately, such transcripts have all but disappeared from Proceedings, since the end of last century.

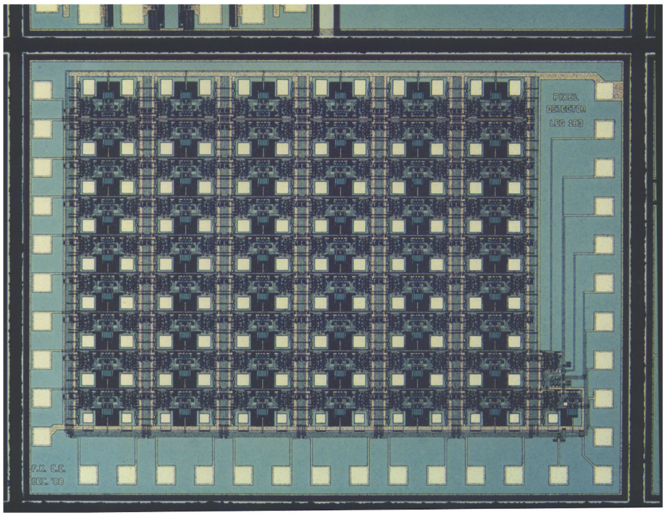

Fig. 3a. The first pixel detector readout chip with pulse processing in each of the 9 × 12 pixels, manufactured in 3 μm SACMOS technology [CERN photo].

Campbell at CERN designed the major parts of the pixel cell and the overall matrix of 16 × 63 pixels, Fig. 4a, which later was designated as 'OmegaD' because of the application as a tracker in the WA94 heavy-ion experiment in the Omega spectrometer. This time, the first measurements indeed could be reported at the 1991 IEEE Symposium (Anghinolfi et al, 1992). These included a test in Omega with a telescopic setup of 3 aligned pixel devices. In Fig. 4b an event is shown, where three tracks are seen crossing all these chips.

In 1990 CERN started the detector R&D program for development of instruments in view of the Large Hadron Collider. The author and colleagues in the LAA team proposed a project, approved as RD19, which aimed at continuing the ongoing LAA efforts towards pixel detectors, but including a larger number of participant universities and institutes, and a wider range of objectives. The RD19 collaboration soon constructed the first complete, operational hybrid pixel detectors, starting with this 'Omega-D′ chip. A series of successively improved readout chips and ever larger systems followed, culminating by 1996 in a 14-plane telescope, which was used in the heavy ion experiment NA57. The installation and exploitation of these new pixel detectors in WA94 and NA57 was strongly supported by Emmanuele Quercigh and Federico Antinori. The results obtained in these running experiments, with a very high density of particle tracks, were key to the acceptance of the pixelated imagers for future installation in the LHC experiments. In the 1996-7 status report of RD19 (Heijne et al., 1997) also results were shown for a second system, in large part designed by the Wuppertal and the Marseille groups led by Karl-Heinz Becks and Pierre Delpierre, and installed as the DELPHI forward tracker (Becks et al., 1998). Towards the end of the RD19 activity in 1999, the CERN team designed the ALICE pixel readout chip (Snoeys et al., 2001). This chip incorporated some of the design strategies for radiation tolerance, and the pixel system based on this chip has been operated in the ALICE inner tracker, until the 2019 LHC upgrade. By 1997 the number of participants in RD19 was in excess of 150, and several of these later became active in commercial companies in the field of imaging.[5] The expertise, shared between the scientists participating in RD19, was the starting point for the design of the pixel arrays in all LHC experiments. It is beyond this introduction to describe the enormous amount of work that took place, mostly in ATLAS

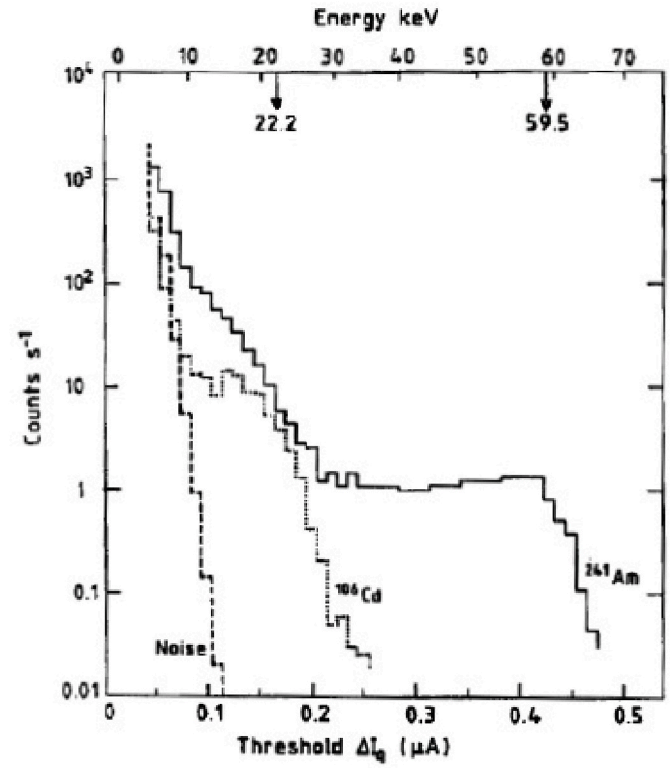

Fig. 3b. Histogram of integral numbers of counts as a function of the comparator threshold, under americium, cadmium or no irradiation (Campbell et al., 1990).

and CMS, and also in ALICE, for better understanding, and fruitful operation of the silicon pixel arrays, consisting of several square meters of sensitive area. The installation of all these instruments was mostly completed by 2008, and it might have appeared as if then no further efforts would be needed. However, the teams soon set out to study future improvements, based on new generations of CMOS chip technology that would allow more complex functions in the pixels. In parallel, based on all this expertise, various radiation imaging detectors were subsequently developed for other applications, in the Medipix collaborations, as well as by several other teams with roots in particle physics. Examples are the team at the Paul Scherrer Institute with Roland Horisberger and Christian Brönnimann; Norbert Wermes and collaborators in Bonn; and the team in Marseille, with Pierre Delpierre. These imagers, designed to study *with* radiation a variety of objects, are discussed in chapter 4.

At this point, some comments may be useful on the continuing competition between hybrid and monolithic technology for radiation imaging. The solder bumping method used for the hybrid matrices originated in the 1970's and cost reduction has been elusive. However, practical advantages continue to make hybridization attractive: complex circuitry with multiple metal layers in different standard CMOS processes, and application-specific choice of sensor material. The main advantages of using monolithic radiation imagers are reduced cost by the absence of the expensive bumps, and thinner material. Therefore, it is thought that monolithic pixel detectors are preferable for future particle trackers. However, it is essential to be aware of trends in industry, where since a few years one seems to go in an opposite direction. Low-cost, wafer-scale copper-copper interconnect has been introduced for imagers, because of desire for ever more complex system circuitry, that can only be implemented in deep submicron (e.g. 26 nm) CMOS. The imager wafer can be made in a more economic CMOS process, and optimized for light sensitivity. A fill-factor close to 100% is achieved with back-side incidence (BSI), if the thickness of the sensor matrix can be reduced to less than 10 μm. Such thinning is done after the Cu–Cu

[5] Several of the chip designers went to the USA, often first working in a university such as Berkeley or Princeton. Then after some years they moved to one of the numerous commercial imager companies. Some of the scientists and engineers ended up working in a European enterprise, a few started a new company.

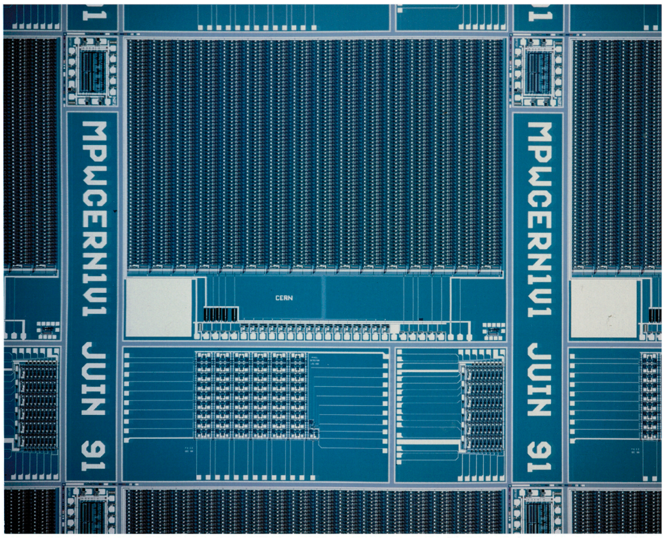

Fig. 4a. Microphoto of the reticle area with 4 chips, on the first RD19 3 μm SACMOS wafer produced in 1991. Bottom-left is the same design as in Fig. 3a, but with enlarged edges, to allow bump-bonding of a sensor [CERN photo].

wafer bonding, as reported e. g at the 2018 IEEE International Solid State Circuits Conference, by Sony (Sakakibara et al., 2018) and Samsung (Kim et al., 2018). With these developments one might begin to consider 'stacked monolithic' particle imagers also for physics applications, in fact a combination of the earlier hybrid and monolithic devices. The advantages of such devices may be overriding, and even if NRE cost may be considerable, it could be acceptable within the overall experiment budget.

4. The Medipix family and similar imagers for science and general applications

Between 1985 and 2000 the new single quantum imagers were primarily developed as silicon tracking and vertex detectors for particle physics experiments, studying charm particles and physics at the future colliders. Quite naturally, it was also tried to image small objects placed in the flux of electrons or X-ray photons, as illustrated in Fig. 5a (Da Via et al., 1997). However, the tracker detectors were not really optimized for imaging of objects, and designs for specific applications were contemplated. A conference on physics and medicine, organized by the Italian physics institute INFN in 1992 in Trieste (Heijne, 1993)

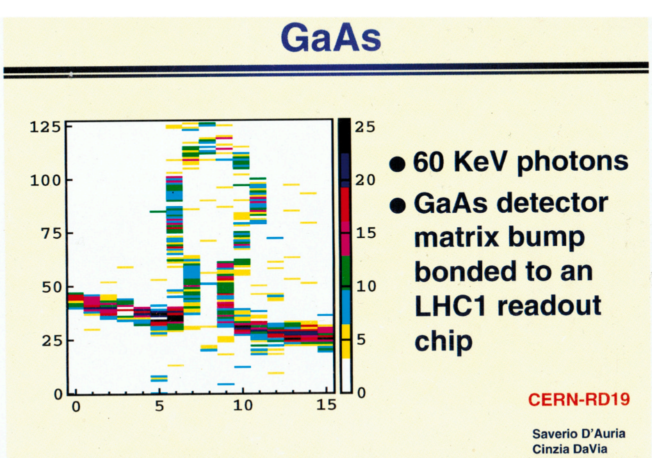

Fig. 5a. Slide from a presentation showing the image of a bent wire, irradiated with an 241 A m radioactive source (Da Via et al., 1997).

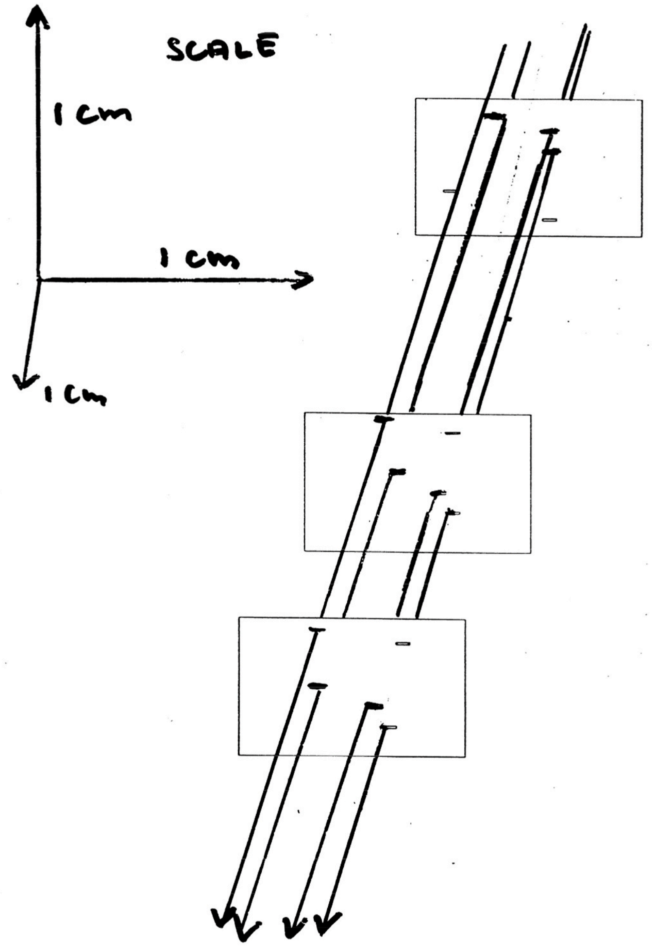

Fig. 4b. Reconstructed image of an event with the 3-chip telescope in Omega. Three particles cross all planes. Pixel size 75 μmx500μm (Anghinolfi et al, 1992).

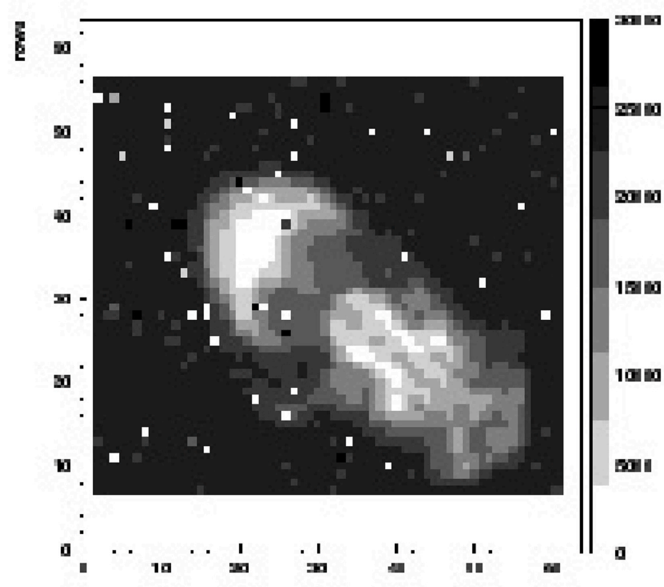

Fig. 5b. Early X-ray image of a dead fly, on the first Photon Counting Chip PCC detector with 64 × 64 pixels [unpublished].

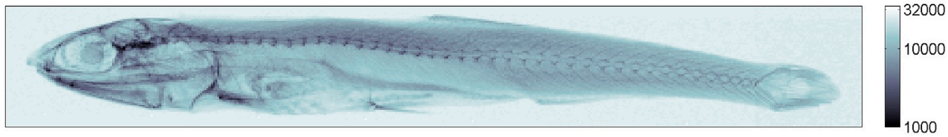

Fig. 6. X-ray image of dried anchovy, using a 17 kV, molybdenum-target X-ray source, exposure time 4 s. Here the full 15-bit depth of the pixel counters in the Medipix1 chip has been used [Tlustos, p.133].

eventually triggered the first Medipix collaboration, promoted by prof. Aldo Stefanini, and which started soon afterwards, involving the CERN team with INFN & Univ. Pisa, and also Univ. of Freiburg and Univ. of Glasgow. The latter two joined because they were active in GaAs detectors, which were deemed to be better adapted to the absorption of the usual ~25 keV X-rays in mammographic medical imaging. Studies of pixel detectors for autoradiography and actual testing with X-rays proceeded prior to the work on a dedicated chip (Amendolia et al., 1996; Amendolia et al., 1997). This Photon Counting Chip (PCC), later called 'Medipix1', aiming at X-radiography was the first design within this collaboration. The readout chip itself, with 64×64 pixels of $170 \times 170 \mu m^2$ was presented at the 1997 IEEE Nuclear Science Symposium (Campbell et al., 1998). Each pixel had a 15-bit counter, taking into account the expected flux in traditional X-ray practice. This counter was implemented as a shift register (Horowitz and Hill, 1989). Peter Fischer had already applied the same approach in the 'MPEC' imager (Fischer, 1996), mentioned hereafter. A VME-based readout system for this Medipix1 was produced by the company Laben S. p.A. in Milano, in collaboration with the Pisa/Cagliari team. The control and readout software was developed by Maurizio Conti in Napoli (Conti et al., 1993). The assembly by bump-bonding of silicon and GaAs sensors soon followed, and one of the first images taken with the Si-Medipix1 is shown in Fig. 5b. With the relatively large pixel size, only few details can be seen, and in the earliest devices there were quite a few dead pixels. However, the detector allowed many exploratory measurements with this previously non-existing method of single quantum imaging (Mikulec et al., 2001). At CERN as well as in the other participating labs several students used this imager, in work for their PhD (Mikulec, 2000; Schwarz, 2001; Bertolucci et al., 2002). Traditional imaging parameters such as contrast, resolution, etc. have been determined, and can be found in these references. Eventually, quite reasonable performance was obtained, although still on a small imaging area, as shown in the X-ray image of an anchovy, Fig. 6, by Lukas Tlustos (2005). This image was a composition of six separate frames, stitched one besides the other. Moreover, Tlustos made a series of exposures, resulting in a movie with dose from the Mo-target X-ray source increasing in steps. Contrast and visibility of details could be studied here as a function of number of hits per pixel, tube current and exposure time. This first imaging detector produced ample experience on which following designs could be based.

The successive phases in the Medipix collaborations will be treated later on, but first is described here some of the parallel work on radiation imaging, by teams that also exploited the progress that was made in pixel detectors for particle physics.

Around 1997, the Bonn and CPPM Marseille teams with Norbert Wermes, Peter Fischer, Pierre Delpierre and collaborators designed the X-ray imager matrix 'MPEC' with 12×63 pixels (Fischer et al., 1998; Fischer et al., 1999), in a similar approach as the CERN PCC. Several projects and iterations in readout chip design and some of the system implementations have been described in chapters 5.4.1 to 5.4.3 of the handbook, already mentioned (Rossi et al., 2006). One example is the XPAD2 project for large pixel detector arrays, to be used in the European Synchrotron Radiation Facility (ESRF) in Grenoble, undertaken by the Marseille group in collaboration with the ESRF (Boudet et al., 2003). This project evolved further over many years, including assemblies XPAD3 with CdTe sensors, in order to improve efficiency at higher photon energies (Cassol et al., 2015).

Another large effort was initiated by Christian Brönnimann, Roland Horisberger and Bernd Schmitt with their team, originally at the Paul Scherrer Institute (PSI) in Switzerland. They started the PILATUS imager project, specifically aiming at X-ray protein crystallography with 12 keV photons produced at the PSI Swiss Light Source (SLS). In 2000 at the 4th Pixel Detector Workshop in Genova, Italy, they reported results with a 22×30 pixel prototype readout chip and assembly (Brönnimann et al., 2001). Over two decades this team developed numerous large systems for synchrotron-based experiments, and established in 2008 a spin-off company.[6] New iterations of different basic readout chips have been called Mythen and Eiger, after other Swiss mountains. An overview of these activities and applications has been published in 2016 (Brönnimann and Trüb, 2016).

In the Medipix family of imaging devices, the Medipix1 was followed a few years later by the Medipix2 readout chip and its hybridized assemblies with silicon, gallium-arsenide GaAs and cadmium-telluride CdTe. A new collaboration had to be created in order to find support and resources for chip design, manufacturing and system construction, and Michael Campbell as spokesman invested a great effort. He describes the achievements of this Medipix2 consortium in 2009, then recounting the 10-year history (Campbell, 2011). Besides the four original participants in Medipix1, another 9, and later even 17 participating institutes (Medipix, 2020) with approximately 70 scientists contributed in many ways. Several are reporting on this work in further articles in the special issue of this journal.

The new chip (Llopart et al., 2002; Llopart, 2007) was 14×14 mm^2 in area, taking a much larger part of the allowed mask area than most other pixel readout chip designs at the time. This allowed a 256×256 matrix of pixels, each with area 55 μmx55μm. The analog front-end amplifier featured the 'Krummenacher' feedback, which could be programmed so as to compensate leakage current degradation and to obtain shorter or longer pulse shapes. More functions now could be accommodated in the pixel, so that this design comes closer to 'quantum processing' instead of simple 'quantum counting'. A window discriminator with lower and upper threshold was implemented and could be tuned, each threshold using 3 bits of the programmable 8-bit configuration register. The two remaining bits enabled masking if the pixel is noisy, and switching to the test input. The discriminated output pulses from the comparator are counted during the active exposure time, and stored in a 13-bit pseudo-random counter, that in fact is a shift register, which facilitates the readout. Readout of the full matrix can proceed with a frequency up to 100 MHz and then takes 9 m s using the serial port. A 32-bit parallel CMOS bus is available as well, which allows readout in 266 μμs. The final version of the chip, designated MPIX2MXR2.0 was made in 2005 with improved thermal stability and radiation tolerance (Campbell, 2011).

Several readout and software systems have been developed for the Medipix2 assemblies by members of the collaboration. The most widely used in the early years was the MUROS2 from Nikhef, Amsterdam, shown in operation Fig. 7a (San Segundo Bello et al., 2003). Again, intensive evaluation was performed by a number of PhD students and team members, now in more institutes than for the Medipix1 detectors. Fig. 8a shows an example of exposure of a Medipix2 in a CERN test

[6] The company 'DECTRIS' with more than 100 collaborators has become by 2019 the largest commercial supplier of hybrid pixel detector systems for scientific photon imaging applications.

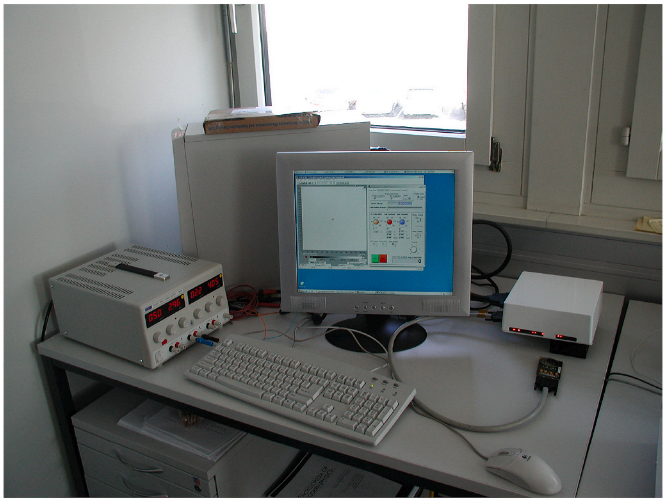

Fig. 7a. A MUROS2 readout box, right, with the small Medipix2 board in front, connected to a PC. The 100 V reverse bias voltage for the sensor is supplied externally by the power supply module, front left. [CERN, 2003 unpublished].

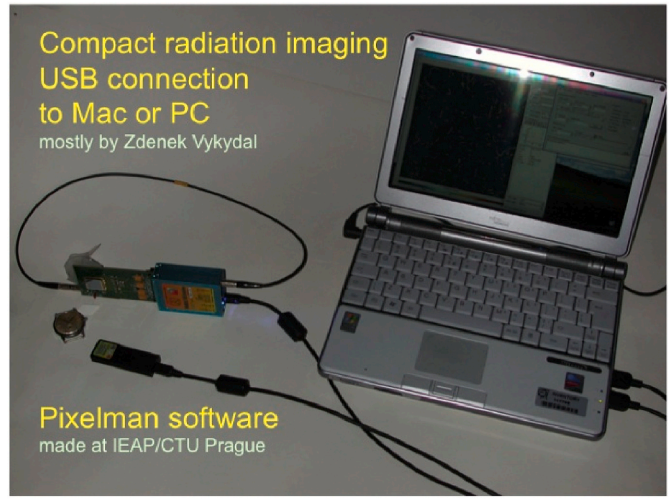

Fig. 7b. Timepix chips mounted as 'standard FITpix', left-behind, or as 'TPXlite', front left, both connected to a MacBook running the Pixelman software. The bias voltage generator is here incorporated in these small boxes. CERN, 2014 (Heijne et al., 2012).

beam, where the pions cross the sensor at a grazing angle. The beam spill time was 2 s, but the exposure time could be shortened electronically to only a few ms for the whole matrix, so as to avoid too many overlapping tracks. The relatively long readout and data recording time on the computer (~1s) resulted in a fairly low efficiency, and from the beginning there have been discussions about improvements in pixel functionality, such as avoiding dead-time by multiple registers. A compromise had to be found between smallest possible pixel size and place for functions, where the availability of sub-micron CMOS technology is a decisive boundary condition. For this particle tracking application the 13-bit counting obviously was not needed, but eventually it was turned to good use, as discussed below. X-ray imaging, on the contrary, needs the full counting depth to achieve good contrast, as is illustrated in Fig. 8b (Llopart, 2007). The quality of the images was improved thanks to finer granularity, larger chip size and lower noise, and new possibilities for application emerged.

One of the notable results was the electronic and visual identification of various types of ionizing radiation by their cluster shapes in the pixel matrix, which led to patenting a new method for radiation dosimetry (Heijne and Pospisil, 2012). The members of the consortium initiated a variety of successful applications, in contacts with established industrial partners or they started new spin-offs. In spite of the name that predominantly suggests exploitation in medical instruments, for a long time the main applications with Medipix2 were in equipment for materials X-ray diffraction, in autoradiography, study of environmental radiation, and in imaging equipment for nuclear reactors and waste storage. However, with more recent chip designs the medical applications see a breakthrough, thanks to new in-pixel functionality. Especially photon energy determination and multiple registers have led to 'color' imaging of different parts in the body, with identification of atomic or molecular composition.

A new chapter was opened with the design of the Timepix chip, taken up within the Medipix2 consortium, and which implemented time tagging in the nanosecond range for incoming quanta in every pixel. This innovation followed when a preliminary test with a Medipix2 without sensor ('naked' chip) had shown that signals could be obtained by using only the metallic bonding pads of the standard pixel readout chip as anode in a gas-filled detector. The original electrons from ionization in the gas drift towards a Gas-Electron-Multiplication 'GEM' foil, with the pixelated anode behind it (Colas et al., 2004). This test was made after discussions over a coffee, about trying a chip as anode in such a gas-filled detector, with Harry van der Graaf, at Nikhef. It may be instructive to underline here the rôle of 'serendipity' in initiating such unexpected developments, and which led to an important step forward. Around 2000 the author was a part-time visiting scientist at Nikhef in Amsterdam, where Jan Visschers and colleagues had just realized their 'MUROS2' readout electronics. In many of the measurements with this system, the full scale of the counters was rarely used. As already mentioned, in testing with a particle beam, most of the pixel counts were zero or one, as shown in Fig. 8a,[7]. So we asked ourselves: could such a large shift-register memory be used for other things? Upon which Jan Visschers suggested: why don't we use it to count clock pulses? Then we can determine the arrival time of the hits and can resolve double counts from overlapping particles. Also, such a chip with built-in time tagging would become an ideal tool to measure drift times in the gas-filled detectors. Jan wrote up a proposal for a new collaboration in which he proposed this new version of Medipix2. The name 'Timepix' was soon introduced. Well aware of the cost of a complete chip iteration, a formal proposal was brought forward within the EUDET collaboration. Funding for this new Timepix chip then was provided in part by EUDET, with strong support by Klaus Desch, Paul Colas, Harry van der Graaf and Jan Timmermans, while the design work and other organizational aspects were taken care of by the Medipix2 collaborators. In a relatively short time, by 2006 the Medipix2 design was upgraded with a clock distribution to all pixels, so that clock pulses could be counted and stored in the shift register (Llopart et al., 2007). Another 'serendipitous' innovation then was the alternative use of this clocking mechanism for signal amplitude measurement, using the Wilkinson-type encoding. Already earlier the desirability of pulse amplitude measurement was expressed by Jan Jakubek and others, and the USB interface for the Medipix2 by Zdenek Vykydal made this possible for large signals, via pickup on the sensor backside. An approximate method was suggested, also for large signals, by making the pixel amplifier oscillate and count the number of swings [see also footnote 7]. Some years before, addressing this issue of in-pixel amplitude measurement, at Nikhef studies had been made by

[7] In the color version of this beam exposure in Fig. 7a it can be noticed that a higher number of counts occurred at the pion interaction vertex, close to the center of the frame. A large energy deposit in this point created a large charge signal. Jan Jakubek in the September 2005 Medipix Collaboration meeting explained this anomalous effect as multiple counting due to oscillation of the amplifier output, with several overshoots going above the threshold value, following the original pulse. He proposed to use this effect as an approximate amplitude measurement. This discussion later prompted Xavi Llopart to implement a proper design for TOT in the Timepix chip.

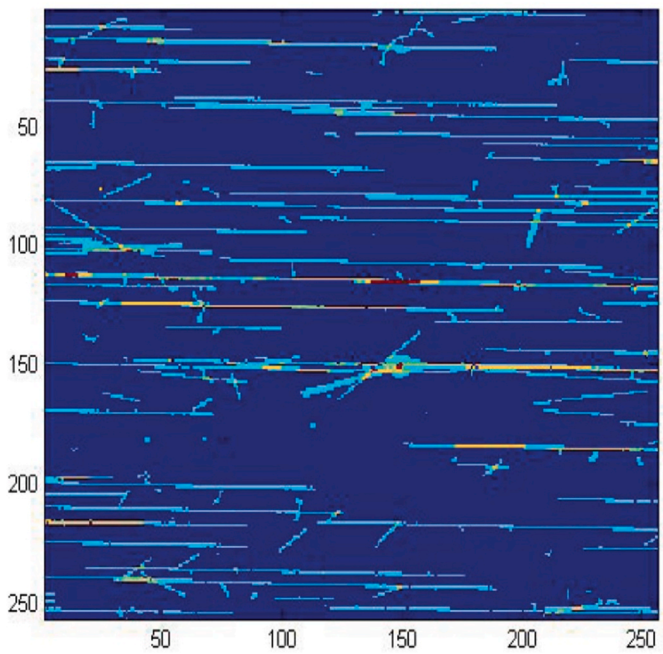

Fig. 8a. Exposure of a Medipix2 with 300 μm Si sensor, in a pion beam at CERN, under grazing angle. Pixels with a single hit are light-blue. Multiple counts (yellow, red) can be seen where tracks have crossed, and at the point where a pion has interacted [CERN, unpublished]. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

David San Segundo Bello, on various schemes for implementing a miniature ADC in each pixel (San Segundo Bello et al., 2001). Now it became reality practically 'overnight', when Xavi Llopart discovered, that it would imply only modest additional logic in his circuit design. The Timepix also has a programmable frame-based exposure, as the Medipix2, but now can be operated in 3 modes. The 'Medipix' hit-counting mode was maintained, but new is the possibility to select for each pixel either Time Of Arrival (TOA) with ~20ns bins or Time Over Threshold (TOT). The energy resolution is 4.5 keV FWHM over a linear amplitude range for Si sensors of 700 to ~200 000 equivalent electrons, or 2.5–700 keV.

In hindsight, it seems somewhat ironic that this introduction of the silicon pixel technology has supported a revival in the world of gas-detectors, which remains in competition with the Si tracking detectors. All this had not been expected, nor planned for, and as said, really was 'serendipitous'. Actually, Medipix and Nikhef thus were among the first to establish that 'naked' chips such as Medipix2 could be used for the detection of electrons in a gas-filled detector (Colas et al., 2004). Fig. 9a shows the spiralling trajectories of two low-energy

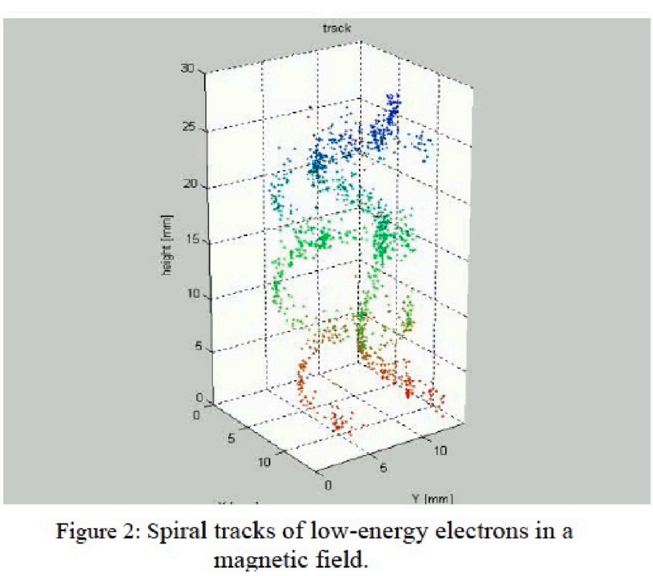

Fig. 9a. A 'naked' Timepix is used as the anode in a gas-filled detector (Gromov et al., 2008). The ionization charges created by the two original electrons are multiplied in a GEM-type structure, that is built on top of the Timepix chips by on–wafer postprocessing.

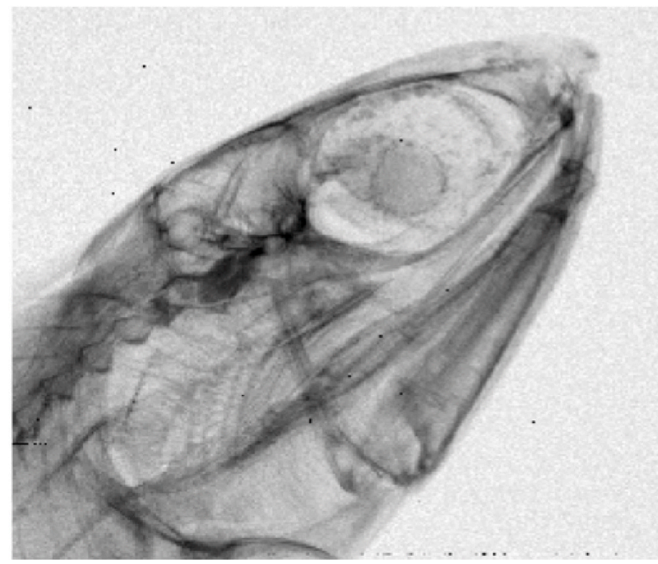

Fig. 8b. Head of the same anchovy as in Fig. 6, now using a Medipix2 assembly with a Si sensor. Much more detail is visible with the 14×14 mm^2 sensor matrix, composed of 256×256 pixels (Llopart, 2007).

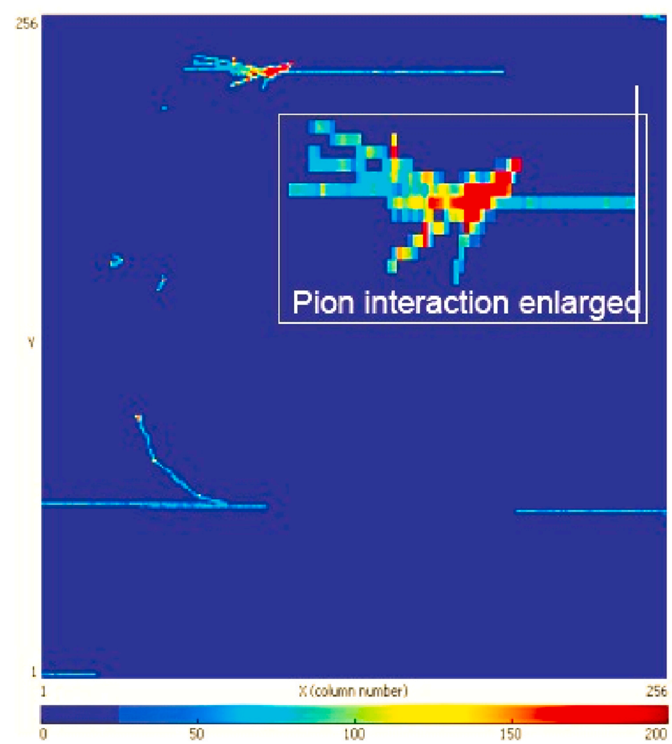

Fig. 9b. Exposure of a Timepix assembly with a 300 μm Si sensor at glancing angle in a 120 GeV pion beam at CERN. An interaction occurs at the top, also shown enlarged. Another pion generates an energetic delta electron which probably comes to rest in the Si, with Bragg peak and high signal amplitude at the end of its trajectory [unpublished].

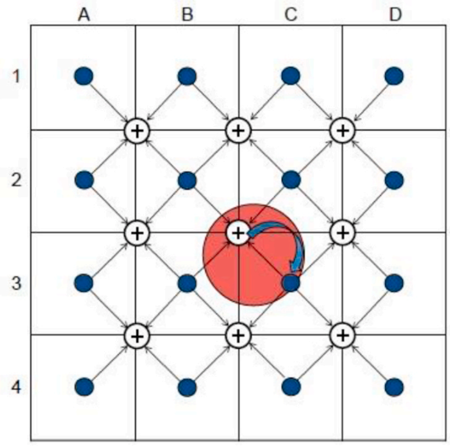

Fig. 10a. In the Medipix3 readout chip the signal charge from up to 4x4 pixels can be summed in real time, and allocated to the pixel with the highest signal. This mode is called Charge Summing Mode 'CSM' (Ballabriga et al., 2007; Ballabriga et al., 2013)

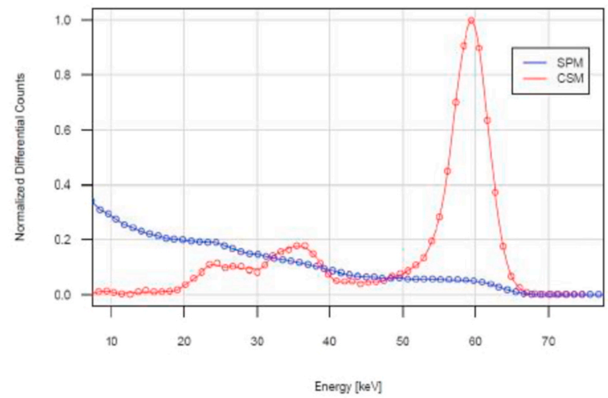

Fig. 10b. Exposure of a Medipix3 with 2mm CdZnTe sensor to a 241Am 59.5keV X-ray source. In Single Pixel Mode 'SPM' the energy spectrum can hardly be seen, but in CSM clear energy peaks become visible. Measurement by Koenig et al. (2013).

electrons in the gas volume in a magnetic field (Gromov et al., 2008). The vertical coordinates have been reconstructed from the timing information, using the calibrated charge drift velocity in the gas. The interest of the amplitude information is illustrated in Fig. 9b, where tracks of 120 GeV pions have been recorded in a beam at CERN. In spite of the minuscule volume of the detector, a fairly complete image of an interaction can be seen, with large energy deposition in the vertex point, including a recoiling nuclear fragment.

In parallel with the development of Timepix, also further miniaturization of the Medipix2 readout modules was actively undertaken by collaborators in the Institute for Experimental and Applied Physics IEAP of the Czech Technical University in Prague. This resulted in the USB interface for Medipix and later in the USB-lite, which also could be used with Timepix, Fig. 7b (Vykydal et al., 2006; Vykydal and Jakubek, 2011; Heijne et al., 2012), which from the outside resembles a memory stick. The small package contains the 65 k cell Medipix2 or Timepix assembly, with all the circuits needed to operate this quantum radiation imager, simply from a USB port. It even includes a 100 V bias supply for the sensor chip. Such modules eventually were also placed on the International Space Station (ISS) and on several satellites in space.

Soon a desire was formulated for better timing precision, mostly in view of Time-of-Flight (ToF) imaging measurements, which allow to discriminate neutrons of different energies, or improve molecular mass spectroscopy, as discussed elsewhere in this issue. Also, the position measurements in the Time Projection Chamber (TPC) gas-filled detectors would profit from faster timing. Gromov et al. (2008) described and tested in 2007 a scheme where a chip-wide 40 MHz clock is complemented with a switchable, voltage controlled local oscillator at 560 MHz, which provides 1.8ns tagging for the first hit in the pixel. The hit signal starts this fast clock, in the final design 640 MHz, which is stopped again by the next leading edge of the general clock, resulting in 1.56ns bins. Two in-pixel registers keep track of the coarse and fine counts and are read out at the end of the exposure. This scheme then became incorporated in the follow-up chip design Timepix3 (Poikela et al., 2014; Frojdh et al., 2015) which became first available in 2013, in the framework of the Medipix3 collaboration.[8] Compared to all previous pixel imaging designs, a significant difference of Timepix3 is the event-driven readout architecture which can be selected in place of the serial frame readout, which remained available. Both ToT and ToA can be registered in each pixel, and as soon as a pixel hit has taken place, these pixel data with its address are queuing up for readout. Now the Timepix3 begins to find many other applications, either 'naked' or with a Si or alternative semiconductor sensor, even back into the field of particle physics, e.g. for recording photons in a Transition Radiation Detector (TRD) or in particle bunch studies in the LHC, where bunches are slightly longer than 1ns and 25ns apart. Moreover, the chip architecture served as prototyping for the VELOpix chip for the upgrade of the LHCb experiment (Poikela et al., 2017), which aims at reading out all pixel hits for all beam crossings at the 40 MHz LHC frequency.

In the meantime, still in the Medipix2 collaboration, design work has been going on Timepix2, an upgraded, frame-based version of the original Timepix. One of the main objectives for this upgrade is the use in space-based radiation measurements, with identification of the incoming quanta. On a satellite, chip operation has to respect the limited bandwidth and power restrictions.

By now, in 2019-2020, a new collaboration, Medipix4 is addressing other long-standing issues in imaging by quantum processing, namely edgeless tiling of the rectangular chips, improvements in energy resolution and still more precise timing for incident quanta. These are currently being implemented in the designs for the Timepix4 readout chip and the Medipix4. Both these chips use a pixel size of the electronic circuits that is smaller than the sensor pixel size, in order to find space in 'lanes', also called 'peripheries' within the matrix for the control and readout functions, and for the Input/Output connectivity with Through-Silicon-Via (TSV). The external connections then can be placed on the back side of the readout chip, and the optional, two-side, edge-periphery for preliminary wafer test can be discarded before the final bump-bonding and assembly

The Medipix4 and the earlier Medipix3 readout chips have been conceived for improved real-time quantum energy resolution at very fine pixel pitch, in a way of solving the issue of charge-sharing, specifically with high flux medical applications in mind, such as energy specific 'color' Computed Tomography 'CT'. The 55μm pixel pitch differentiates Medipix3 from other approaches which have pixels between 300um and 500um and no compensation for charge diffusion or fluorescence, but which admittedly is somewhat less needed with such larger pixel sizes. Smaller pixels still can process single quanta in a higher incident flux, and also have the advantage of a stronger 'small-pixel-effect' which consists in signal induction by electrons only, eliminating the variable influence of partial hole collection

While the Medipix4 is still under development, the first prototype of Medipix3 (Ballabriga et al., 2007) was available in 2006 and the full chip upgraded with some corrections, Medipix3RX was produced by 2011 (Ballabriga et al., 2013). The essential characteristic of these chips

[8] The cycle time for chip generations depends on several boundary conditions, of which in a scientific research environment the funding and manpower resources are most critical. It can be noted that science applications have difficulty to keep track with the CMOS technology nodes, which one after the other support progress and profitable industrial exploitation.

Table 1
Generations of Medipix radiation imagers.

	year	pixel size, matrix	CMOS	in-pixel		readout	tiling
				# transist	some functions		# sides
Medipix	1998	170 µm 64 × 64	1 µm	400	counting > threshold	exposed frame	3
Medipix2	2003	55 µm 256 × 256	0.25 µm	530	counting in window	exposed frame	3
Mpix2MXR20	2005	55 µm 256 × 256	0.25 µm	530	counting in window	exposed frame	3
Timepix	2007	55 µm 256 × 256	0.25 µm	550	20nsTOA or TOT	exposed frame	3
Medipix3	2009	55/110 µm 256 × 256	0.13 µm	1800	c + charge summing	read/write frames	3
Medipix3RX	2011	55/110 µm 256 × 256	0.13 µm	1700	c + charge summing	read/write frames	3
Dosepix	2011	220 µm 16 × 16	0.13 µm	22000	16 energy bins	3 exposure modes	3
Timepix3	2013	55 µm 256 × 256	0.13 µm	2700	1.5ns TOA + TOT	+hit driven	3
Timepix2	2018	55 µm 256 × 256	0.13 µm	1900	10ns TOA + TOT + PC	RW exposed frame	3
Timepix4	2019	55 µm 512 × 448	65 nm	5300	<0.2ns TOA + TOT	+hit driven	4
Medipix4	2021?	tbd	0.13 µm	tbd	c + charge summing	read/write frames	4

is the inter-pixel communication, allowing real-time summing of signals around a hit pixel. This scheme permits spectroscopic X–ray imaging without the need to send all hit data off-chip, so that a higher rate of incident X-rays can be processed as single quanta. The algorithm is illustrated schematically in Fig. 10a, and avoids the loss of below-threshold fractions of the energy of the incoming quantum, and at the same time obtains the best approximation of the total energy deposited by the incoming quantum. The beneficial effect of this method is shown in Fig. 10b (Koenig et al., 2013).

The CERN 'Medipix' team designed several other pixel readout chips during the past two decades, such as the Dosepix (Wong et al., 2011) and also prototype chips for future physics experiments[9] (Valerio et al., 2014). This 'family' of developments has been described in great detail by Rafael Ballabriga, Michael Campbell and Xavi Llopart (Ballabriga et al., 2018). Much of the recent work, obviously will be treated in other contributions to this special journal issue. In Table 1 a condensed summary is provided of the successive 'Medipix' radiation imagers. The increase of complexity can be judged from the number of transistors in the unit pixel, fifth column, increasing from 400 to 5300 in Timepix4. Some of the in-pixel functions are recalled. The Dosepix stands out with much large pixels, and the possibility to record the analog information in 16 adjustable energy bins.

To conclude this section, it is progressively becoming clear that spectroscopic, color-discriminating imaging based on single quantum processing will play an important rôle in future analytical and medical instruments. Katsuyuki (Ken) Taguchi and Jan Iwanczyk developed a vision for the next decade (Taguchi and Iwanczyk, 2013), where this imaging method definitely comes on the scene. Computed Tomography CT as well as X-ray images now begin to provide molecular information about the object. Worldwide, there may be at this time about ten groups working on slightly different approaches. Ballabriga has made an effort to review technical details of published work (Ballabriga et al., 2016) and a series of bi-annual workshops is being held at CERN to discuss detector progress and applications. The initiating rôle of CERN is explained by the necessity to work with single quanta in elementary particle physics, which gave rise to the semiconductor micro-pattern/imaging pixel detectors in the first place.

5. A future with big data

It is satisfying to note the development of a wide range of applications for single quantum semiconductor imaging detectors, now 30 years after the first tentative discussions at the 1988 Leuven Workshop, and 20 years into the series of International Workshops on Radiation Imaging Detectors, which started in 1998 in Sundsvall. These instruments have profited from the incredible progress in silicon device technology. It can be expected that nanoelectronics, or even picoelectronics technology will continue to create new opportunities for radiation imaging. The first condition for fulfilling this expectation is to carefully study where the chip industry is heading to, and try to understand and master the use of their technologies. The integrated circuits that are used in particle physics and other radiation imaging, are often quite different in architecture and layout, compared to the majority of the chips for commercial applications. Therefore, intimate knowledge of the technology is needed, to avoid incompatibilities, and to optimize designs to the specific needs. Radiation tolerance is needed for the readout part, but radiation sensitivity must be retained in the imaging elements. Given the investment cost for the most recent nano IC technologies[10] commercial interests become so preponderant that little technical details are published. Then it becomes more difficult to imagine unusual implementations. A second condition, now on the side of physics users, will be the availability of sufficient resources to grant access, to finance the ever increasing cost of new technology generations and to maintain expertise in circuit design and evaluation. The complexity of nanometer technologies is becoming extreme and requires equally complex tools for the design process.

Guessing about future technology aspects of our imagers, it looks obvious that both the overall area will increase using edgeless tiling, and the basic pixel dimensions will be reduced, but with the option of grouping them into larger units, as required by the application at hand. If greater flexibility could be integrated in the architecture, this might allow a larger production volume for the same chip, and lead to significant cost reduction. One might dream of Application Programmable Imaging Matrices (APIM) along the lines of Field Programmable Gate Arrays (FPGA).

In industry today, the emphasis on innovation is not only in making ever smaller transistors, but now increasingly on adding sophistication in the devices, by stacking of multiple layers with different levels of functionality. For example, robotics apparatus requires imaging combined with distance determination, and it is desirable that both a laser-emitter and a rangefinder can be integrated with the imager. The use of multi-layer pixel imager assemblies has already been experimented by the Perugia team (Passeri et al., 2014) in the VIPIX project, and in collaboration with Fermilab (Yarema et al, 2013), but much more development would be needed to achieve the desired functionality with appropriate reliability, and at acceptable cost. Industrial imagers, even with pixel size of one µm or below (Kim et al., 2018), today are beginning to integrate some of the signal processing in the thin, even <10 µm, sensor layer, and added functionality such as individual ADC, in a support wafer, bonded together with electrical contacts to each sensor pixel

[9] The chips for physics experiments now in return draw on the expertise from work on Medipix but are funded separately, by the physics teams.

[10] The Taiwanese company TSMC announced to invest 19 billion US $ for their new 5 nm manufacturing facility.

at a 6 μm pitch (Sakakibara et al., 2018). Digitization of the signals then is performed directly on the sensor, rather than in a separate processor or off-line. TSV technology eventually may allow even more than two layers, with added functions inside the assembly. Continuously, there will be discussion on trade-off between information processing on-chip and transmission to off-chip standard computing. The pixel dimensions tend to become smaller, but if intelligent pixels are preferred, these would take a larger area (Ballabriga et al., 2019). Besides cost, the main technical factors will be the volume and rate of raw data, power comparison between local processing and transmission, and cooling possibilities on-chip. Cooling will become an ever more important issue, and might be solved by channels inside the device and an evaporative cooling medium, such as CO_2. Active developments are ongoing on such microchannel cooling, and will be applied, for example, in the upgrade of the LHCb pixel instrument (Agular Francisco et al., 2015).

Another area of development for the single quantum imagers is the extension of the electromagnetic frequency bands by different types of sensor structures. And the same for particles such as neutrons, molecules, and, who knows, dark matter quanta. The possibilities of single quantum imaging for astronomy are just beginning to be discovered. Several innovating, large institutes are proposed or being constructed for imaging work with neutrons, such as the European Spallation Source ESS in Lund, Sweden. These may become important users of quantum imagers.

Overall, it can be expected that quantum processing imagers will generate massive amounts of data, because of increased speed, larger areas covered, ever smaller pixels and more information coming from each pixel. Expertise will have to be created for effective and economic use of these instruments. Optimization of the trade-off between functional integration in the instrument itself and the off-line data processing is one aspect. The similar trend to ever-smaller, ever more numerous pixels has already improved the quality of imaging in the visible, and small details can be recognized even in large pictures, taken, for example, from outer space. The deluge of 'big-data' resulting from this trend has led to the need for lots of additional electronic activity, in processing, in storage and in transmission. Hopefully, in our case initiatives for self-learning analysis software will come to the rescue, in much the same way as we humans learn to see with our own eyes. It just takes 2–3 years of training, and billions of people manage this very well.

Finally, the expertise gained with the quantum imaging devices directly returns profit to the particle physics community by providing high level, excellent technology teams, who can fulfill the difficult requirements of new experiments.

Declaration of competing interest

The author declares that he has no competing financial interests in this work beyond the regular salary from his employers. Numerous personal relationships have influenced the work reported in this paper.

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