

# Future Directions of Pixel Detectors and their Applications in Life Sciences

Jan Jakůbek

Institute of Experimental and Applied Physics, Czech Technical University in Prague

## Outline

#### Introduction

- Radiation imaging
- Imaging pixel detectors (particle counting) Pilatus, Medipix2 and Timepix

#### Applications of pixel technology - Imaging

Life science

Institute of Experimental and Applied Physics Czech Technical University in Prague

And some others

#### **Problems of current devices**

- Charge sharing deteriorates spectrometric performance
- Dead-time between exposures

#### Future directions (with respect to applications)

- Higher complexity of pixel cells more functionality (Medipix3 concept)
  - Separate event by event processing tracking (*Timepix2 concept*)





Energy [keV]

400







### **Radiation imaging = Radiography**

#### Radiography (film) or radioscopy (digital) = Imaging of (internal) sample structure using radiation

#### Radiation source is placed outside of a sample:

- Absorption radiography recording intensity change
- Energy changes
- Phase contrast imaging
- Diffraction imaging, ...

#### Radiation originates in a sample body:

- Autoradiography using isotopic marker (PET, SPECT, ...)
- Autoradiography of activated sample (e.g. neutron activation)

#### **Combination of both approaches:**

- Prompt gamma imaging (excitation by neutron beam)
- X-ray fluorescence (excitation by X-rays, gammas, heavy particles, ...)

#### **Multimodal imaging**

Wilhelm Conrad Roentgen showed that bones could be visualized by X-raying his wife's hand in 1895





### Imaging detectors of radiation (for radiography)

Film emulsions change of chemical or physical properties after interaction with radiation. Needs special treatment (developing process, scanning,).	Cl loni cha an (C(	harge integrating devices izing radiation creates irge which is collected d integrated in pixels CDs, CMOS sensors, Flat panels,)	Single particle (counting) pixel detectors Ionizing radiation creates charge which is compared with threshold and registered digitally in pixels
Very high resolution + Low noise Cheap	Hi	➡ gh spatial resolution Low price	 Good spatial resolution + High read-out speed No noise, no dark current Unlimited dynamic range
Nonlinear response – Limited dynamic range Needs processing	Lii	Dark current – Noise mited dynamic range	- ?

Jan Jakůbek



## Particle counting pixel detectors



FNAL, 26th September 2008

Institute of Experimental

Jan Jakůbek



## **Applications:**



Jan Jakůbek



# High resolution X-ray radiography:



### High resolution X-ray radiography: Detector response has to be known !!



- Energy spectrum differs from
  point to point
- Dependence of efficiency on the energy has to be known for each pixel !!

#### Daisy blossom (almost transparent for X-rays)



### High contrast X-ray imaging: Example: Living mouse



X-ray transmission Single image of mouse head

(dose 0.9 mGy)

Single photon counting device can count unlimited number of photons, noise in images is given just by poissonian statistics:

- => Unlimited number of gray levels in images depending just on the beam intensity and exposure time.
- => Almost unlimited contrast



### High contrast X-ray imaging: Example: Living mouse 2





FNAL, 26th September 2008

Jan Jakůbek

### High resolution X-ray tomography: Mouse bone structure





#### FNAL, 26th September 2008

Jan Jakůbek

#### High contrast X-ray tomography: Mouse kidney

Frame

Object

Mylar foil

(3.8µm)



- 90 projections, 20 seconds each =>1800 s = 30 min => too much (drying causes significant changes)
- Drying avoided by placing object into the frame between two thin mylar foils.
  - Projection of the holding frame overlaps the object for several angles => just 72 angles are usable.

#### No contrast agent used !

### High contrast X-ray tomography: Mouse kidney - result





FNAL, 26th September 2008

Jan Jakůbek



Institute of Experimental and Applied Physics Czech Technical University in Prague

# **Applications:**

### **Biology: Leaf Miner story**

(skip)

FNAL, 26th September 2008

Jan Jakůbek

### High resolution X-ray radiography: Example: Leaf Miner story



Leaf miner (*Cameraria ohridella*) - small moth. In larvae stadium it lives inside of chestnut tree leafs making "mines" and causing serious problems to the tree. Indication: chestnut leafs get brown, dry and fall down early.



### High resolution X-ray radiography: Example: Leaf Miner story



Worms are growing up and after three feeding instars larvae build-up a silken cocoon (pupae)



FNAL, 26th September 2008

Jan Jakůbek

#### High resolution X-ray radiography:



### **Example:** Leaf Miner story - Cure

The best cure: natural enemy (parasitic wasp) Certain small wasps can put eggs into leaf miner pupas Parasite inside of parasite:







Parasite kills the pupa and leaves it as adult wasp



![](_page_17_Figure_0.jpeg)

Institute of Experimental and Applied Physics Czech Technical University in Prague

# **Applications:**

#### **Phase contrast imaging**

![](_page_17_Picture_4.jpeg)

Jan Jakůbek

![](_page_18_Picture_0.jpeg)

#### X-ray phase contrast imaging: Edges are enhanced in radiograms

![](_page_18_Picture_3.jpeg)

Jan Jakůbek

### **Physical applications:**

![](_page_19_Picture_1.jpeg)

# Phase contrast imaging

- Changes of X-ray wave passing a sample are described by the **complex index of refraction**  $\mathbf{n} = \mathbf{1} - \delta - \mathbf{i} \beta$ 
  - The **phase term**  $\delta$  contains refractive effects (causing **phase shift**  $\phi$ ). Material inhomogeneities in the object produce changes in the **phase**  $\delta$ .
- Phase contrast imaging:  $\delta \sim 1/E_{v}^{2}$
- Absoption imaging:  $\beta \sim 1/E_{v}^{4}$
- For X-rays in light elements,  $\delta$  can become orders of magnitude greater than the absorption term  $\beta$ . Thus, **phase contrast** can be observed while <u>absorption</u> contrast may be negligible.

![](_page_19_Figure_8.jpeg)

### **Physical applications:** In-line Phase Contrast Imaging

Spatial coherence ensured by small size of radiation source (point source):

- X-ray: Microfocus X-ray tube
- Thermal neutrons: pinhole aperture

![](_page_20_Figure_4.jpeg)

![](_page_20_Picture_5.jpeg)

**B)** Phase enhanced image taken by Medipix2 at distance of 60cm revealing fine internal structure

In-line phase enhanced imaging with microfocus X-ray tube. In the intensity profile it can be seen that signal caused by phase shift (B) is significantly larger than signal caused by intensity attenuation (A). Intensity profile was measured with a 1mm thick and 160µm wide PE foil and tungsten X-ray tube at 40kV, L=60cm.

tube

30µm

FNAL, 26th September 2008

Jan Jakůbek

![](_page_20_Picture_12.jpeg)

160µm PE strip

![](_page_20_Figure_13.jpeg)

R

![](_page_20_Figure_14.jpeg)

![](_page_21_Figure_0.jpeg)

Institute of Experimental and Applied Physics Czech Technical University in Prague

# **Applications:**

### **Neutron transmission radiography**

(skip)

![](_page_22_Picture_0.jpeg)

# **Neutron Radiography**

- While X-rays are attenuated more effectively by heavier materials like metals, neutrons allow to image some light materials such as hydrogenous substances with high contrast.
- Neutron radiography can serve as complementary technique to X-ray radiography

![](_page_22_Picture_4.jpeg)

![](_page_22_Picture_5.jpeg)

X-rays

#### Neutrons

(courtesy NEUTRA facility at PSI)

In the X-ray image, the metal parts of the photo camera are seen clearly, while the neutron radiogram shows details of the plastic parts.

# CCD camera with scintillator filled by converter material

![](_page_23_Picture_1.jpeg)

#### **Offers:**

- Good efficiency
- Large field of view
- Digital output
  > OK for tomography

#### But:

- Low spatial resolution
- Dark current
- => Limited exposure time
- => Limited dynamic range

A flower was measured through a "wall of granite bricks" and shows a fascinating high contrast (compared to the stones) because of the strong attenuation of the involved hydrogen.

![](_page_23_Picture_12.jpeg)

#### (courtesy NEUTRA facility at PSI)

FNAL, 26th September 2008

Jan Jakůbek

![](_page_24_Picture_0.jpeg)

# Neutron radiography with Medipix coated by <sup>6</sup>LiF: **Samples: Blank cartridge**

![](_page_24_Figure_2.jpeg)

Jan Jakůbek

![](_page_25_Picture_0.jpeg)

### Neutron radiography with coated Medipix: Samples: Glued Al pieces

# Glue raised through capillary attraction

![](_page_25_Picture_3.jpeg)

![](_page_25_Figure_4.jpeg)

70

![](_page_26_Picture_0.jpeg)

# Neutron radiography with coated Medipix2-Quad: Wrist watch

![](_page_26_Picture_3.jpeg)

![](_page_26_Picture_4.jpeg)

![](_page_26_Picture_5.jpeg)

![](_page_26_Picture_6.jpeg)

Exposition time = 500 seconds

FNAL, 26th September 2008

Jan Jakůbek

![](_page_27_Picture_0.jpeg)

## **Neutron microtomography**

Blank cartridge Explosive filling clearly visible

![](_page_27_Picture_3.jpeg)

Taken 100 projections 150 seconds each. Reconstruction using filtered back-projection algorithm.

![](_page_27_Picture_5.jpeg)

![](_page_28_Picture_0.jpeg)

## **Neutron microtomography**

![](_page_28_Picture_3.jpeg)

![](_page_28_Picture_4.jpeg)

Taken 100 projections 150 seconds each. Reconstruction using filtered back-projection algorithm.

![](_page_28_Picture_6.jpeg)

Institute of Experimental and Applied Physics Czech Technical University in Prague

# **Applications:**

### **Radiography with highly ionizing particles**

(skip)

![](_page_30_Picture_0.jpeg)

#### Application: Radiography with highly ionizing particles

![](_page_30_Figure_2.jpeg)

- With common sources of heavy charged particles (isotopes, ion beams) it is feasible to inspect just small (thin) objects (thin layer, foils, cellular structures)
- Precision of thickness measurement can be in nanometer scale.

![](_page_31_Picture_0.jpeg)

### Need of per pixel energy measurement: TimePix and its TOT mode

Counter in each pixel can be used as

- **Timer** to measure detection time => TOF experiments, TPC detectors, ...
- Wilkinson type ADC to measure energy of each particle detected.

![](_page_31_Figure_5.jpeg)

![](_page_32_Picture_0.jpeg)

# **Charge sharing effect - clusters**

- Ionizing particle creates a charge in the sensor.
- The charge is collected by external electric field => the process takes some time
- Due to charge diffusion the charge cloud expands
- The charge cloud can overlap several adjacent pixels => CLUSTER
- Pixels in a cluster will detect the charge if it is higher then certain threshold

![](_page_32_Figure_7.jpeg)

- Particle Energy
- Depth of interaction
- Detector Dias Voltage

Ionizing particle can creates huge charge signal in several adjacent pixels forming cluster. Cluster volume depends on particle energy.

![](_page_32_Figure_12.jpeg)

![](_page_32_Figure_13.jpeg)

Energy threshold

### TOT mode calibration: Why to calibrate?

![](_page_33_Figure_1.jpeg)

If particle hits a border between pixels then:

- $\Rightarrow$  charge is collected by more than one pixel
- ⇒ to recover original charge it is possible to sum energies measured by all hit pixels (compute cluster volume)

# **Test without calibration**: <sup>241</sup>Am: 59.5keV, 26.3keV

For 59,5keV are two and three pixel clusters more frequent then singles.

![](_page_33_Figure_7.jpeg)

### TOT mode calibration: How to calibrate?

![](_page_34_Picture_1.jpeg)

Test pulse

Gamma or X-ray sources taking into account just single pixel clusters.

=> charge leak to adjacent pixel is under threshold

![](_page_34_Figure_5.jpeg)

![](_page_35_Picture_0.jpeg)

#### TOT mode calibration:

### **Surrogate calibration function**

![](_page_35_Figure_3.jpeg)
### TOT mode calibration: Per pixel calibration



To improve energy resolution per pixel calibration is needed.

- Calibration done using 5.9keV (Fe55), 15.8keV (Zr) and 59.5keV (Am241) using single pixel clusters.
- Good per pixel spectra of one pixel clusters needed => 200 000 000 clusters analyzed in case of Am241.
- Gaussian fit done for each peak and each parameter => 200 000 gaussians
- Just three parameters determined for each pixel: *a*, *b* and *t*.
- Parameters *c* and *d* were set constant to 2.4 and 1 respectively.



#### Zr (15.8keV):









**Physics** 

Unive

zech

IEAP - CTU Prague 37

Jan Jakůbek



### TOT mode calibration:

### Tests with per pixel calibrated TimePix





### **Small digression**

# XRF Imaging ...

### ... event by event processing

FNAL, 26th September 2008

Institute of Experimental and Applied Physics Czech Technical University in Prague

Jan Jakůbek

#### X-ray fluorescence imaging ? Experimental setup and samples



### Institute of Experimental and Applied Physics Czech Technical University in Prague **Piece of PCB** Sample X-ray tube Characteristic radiation Pin-hole collimator **Pixel detector**

#### **One Euro coin**

Jan Jakůbek

#### X-ray fluorescence imaging: **Results**





#### Color coding: **Cu** = Red, **Pb** = Green, **Sn** = Blue



#### Color coding: Zn content is displayed in Pink

FNAL, 26th September 2008

Jan Jakůbek



### **Another digression**

### Energy sensitive X-ray transmission imaging with TimePix device ...

### ... event by event processing

FNAL, 26th September 2008

Institute of Experimental and Applied Physics Czech Technical University in Prague

Jan Jakůbek



#### X-ray transmission radiography: Material recognition

- Energy dependence of X-ray absorption is given by the material composition => recognition
- Recognition is simpler for materials with edges in absorption spectra, often just several energy windows are needed
- Absorption spectra of soft biological materials differ just slightly => real per pixel spectroscopy is needed.



#### Can we recognize them?

Transmission difference 0.60% Water-Plex 0.50% Water-Fat 0.40% Transmission difference [%] 0.30% 0.20% 0.10% 0.00% 5.0 15.0 20.0 25.0 30.0 35.0 40.0 -0.10% -0.20% -0.30% Energy [keV]



FNAL, 26th September 2008

Jan Jakůbek

#### X-ray transmission radiography: Soft tissue recognition

- Phantom sample made of Plexi glass and water
- Irradiated with tungsten X-ray tube at 40kV and just 2uA
- Integral intensity image shows very low contrast
- Per pixel transmission spectra recorded in each pixel (80000 frames a 1ms => 80 sec exposition

Measured transmission difference (normalized)



Plexi glass

(5 mm)

Cluster analysis - Const volume cluster count 005.txt

Water (~3.2 mm)







Jan Jakůbek

IEAP – CTU Prague 44

0.5

-0.5

Diff. [%]



(skip)

Jan Jakůbek



### TOT mode calibration: Heavy charged particles?





### Heavy charged particles: **Subpixel resolution**



Cluster shape depends on detector bias voltage. For low bias a diffusion dominates => Gaussian cluster shape



- $\Rightarrow$  Subpixel resolution is be reached by Gaussian fit.
- $\Rightarrow$  Spatial resolution for 10 MeV alphas is 320 nm !!



Vbias=7.2V

University in Prague **Applied Physics** 

and

**nstitute of Experimental** 

**Czech Technical** 



#### **Spatial resolution determination:**

### Spatial resolution as a function of energy

 LASER test performed for different equivalent energies of 50keV, 120keV, 1.2MeV, 3.2MeV and 9.9MeV



Clusters of Scan step 5um (22 x 22 steps) frame=7 cluster=0 (center=[125.561, 126.32] volume=3104



FNAL, 26th September 2008

**Applied Physics** University in Prague

and

Institute of Experimental

**Czech Technical** 

Jan Jakůbek



### Radiography with heavy charged particles: Example with TimePix



 <sup>241</sup>Am alpha source used
 Set of Mylar foils used to attenuate energy
 Measurement performed in vacuum









#### Radiography with heavy charged particles: Determination of longitudinal precision





#### Radiography with heavy charged particles: Sample object: Spider skin (slough)

Jan







# Radiography with heavy charged particles: Sample object – Spider skin (slough)



16 x (1 Mpixels) ~0.7 particles per pixel



Institute of Experimental and Applied Physics Czech Technical University in Prague

# **Applications:**

### Tracking of heavy charged particles (Timepix as a Bragg detector)

(skip)



# **Proton tracking**

Institute of Experimental and Applied Physics Czech Technical University in Prague

Tandetron facility (Řež) used for basic tests.
Defocused proton beam (low intensity).
TimePix with positioning in vacuum chamber







## **Proton in Silicon**

- Energy losses defined by Bragg curve => model needed
- The charge is collected from different depths
- Bias voltage set to 7.2V = > diffusion dominates = > Gaussian charge spread





### **Bragg curve modeling**

- Stopping power of Silicon for protons is characterized by surrogate functions (see inset in chart below)
- By its integration the energy profile along the track is determined as a function of initial energy.



#### Bragg curve:

 $E(x) = -c((E_0 - a)^{1-e} - c(1-e)x)^{\frac{e}{1-e}}$ September 2008



### **Clusters and fits**



FNAL, 26th September 2008

Jan Jakůbek



**Applications:** 

### (Very) Low energy physics Detection of ultra-cold neutrons



FNAL, 26th September 2008

Institute of Experimental and Applied Physics Czech Technical University in Prague

Jan Jakůbek



#### **Detection of ultra cold neutrons**

Ultra-cold neutrons (UCN) are neutrons with small kinetic energy (~300 neV). The energy is so small that they are totally reflected from the surface of most materials under any angle of incidence so they can be trapped by the effective Fermi's material potential. This energy corresponds to a velocity of less than 7 m/s, an effective temperature of 0.005 K or wavelength of about 1000 Å.

UCNs can be stored in "bottles" for times approaching the  $\beta$  decay lifetime of the neutron (~ 900 s).

 Experiments with bottled UCN can offer orders-of-magnitude improvement for various precise measurements of neutron properties that are sensitive to physics beyond the standard model.

 UCNs are generated in several world laboratories (<u>ILL Grenoble</u>, <u>Los Alamos NL</u>, <u>PSI Villigen</u>,...).



# **Detector design**

- The pixel detector <u>TimePix</u> working in its TOT mode allows to detect heavy charged particles with very high <u>subpixel spatial resolution</u>.
- This feature can be used for precise detection of UCNs via their conversion to heavy charged particles.
- The conversion can be performed in layer of <sup>6</sup>Li (in form of <sup>6</sup>LiF) or <sup>10</sup>B deposited on the sensor surface. Since energy of UCN is very low, the cross-section of both materials for UCN capture is extremely high and conversion layer can be very thin.

#### <sup>6</sup>Li: <sup>6</sup>Li + n $\rightarrow \alpha$ (2.05 MeV) + <sup>3</sup>H (2.72 MeV)





### **Monte-Carlo simulations**

Institute of Experimental and Applied Physics Czech Technical University in Prague



• Aim: To estimate detection efficiency and spatial resolution



Expected UCNs velocity: 500 cm/s. For such neutrons the cross section of <sup>6</sup>Li increases to **0.34 Mbarn**. The cross section of <sup>10</sup>B reaches **1.67 Mbarn**.

50% of such UCNs are fully absorbed in <sup>6</sup>LiF layer of 85 ug/cm<sup>2</sup> (~ 320 nm thickness). For <sup>10</sup>B it is layer of 7 ug/cm<sup>2</sup> (~ 30 nm thickness).

Used <sup>6</sup>LiF density of 2.65 g/cm<sup>3</sup> and <sup>10</sup>B density of 2.35 g/cm<sup>3</sup>.

#### Geometry used in simulations



### Simulation results for <sup>6</sup>LiF



The converter thickness maximizing efficiency is about 1.5 um thick. Resulting efficiency is 81% for Si layer of 0.15 um resp. 71% for Si layer of 1 um.



Dependence of spatial resolution (in terms of FWHM of PSF) on thickness of <sup>6</sup>LiF coating. The resolution for 1.5 um thickness is about 4.1 um for Si layer of 0.15 um resp. 6.4 um for Si layer of 1 um.



### Simulation results for <sup>10</sup>B





The converter thickness maximizing efficiency is about 1.5 um thick. Resulting efficiency is 89% for Si layer of 0.15 um resp. 61% for Si layer of 1 um. The resolution for 1.5 um thickness is about 1.6 um for Si layer of 0.15 um resp. 3.0 um for Si layer of 1 um.

0.4

Thickness [um]

0.6

**Spatial resolution** 

0.2



0.8



### **Experiment 2: Deposited layer of <sup>6</sup>LiF**

- 400 ug/cm<sup>2</sup> of <sup>6</sup>LiF was deposited onto Timepix sensor surface by evaporation (~ 1.5 um).
- Spectrum was measured and compared with simulation (thickness of insensitive Si layer tuned to achieve the best agreement).



The insensitive layer thickness is ~ 1 um.
Detection efficiency ~ 70%.



# **Spatial resolution**

Straight edge made of stainless steel (50 um thick) placed on detector surface.
 Positions of all detected clusters evaluated with subpixel precision.



A spatial resolution of **2.3 \mum** (sigma of the error function) was measured this way. This result corresponds to 5.3  $\mu$ m of FWHM of point spread function.

 The method is very promising for many experiments with UCNs => it is supported by ILL project <u>PF2 UCN 3-14-239</u> (got 25 days of beam time for 2008).



### **Transparency depends on UCN energy**





### Time Of Flight measurement = Position sensitive neutron spectroscopy



# Position sensitive TOF spectroscopy of UCNs

15 um thick stainless











Jan Jakůbek



# Summary:

### **Issues of current devices**

Jan Jakůbek

### Issues to be solved: Particle counting – charge sharing





### Issues to be solved: Dead time



Institute of Experimental and Applied Physics Czech Technical University in Prague





Continuous operation i.e. TWO COUNTERS in each pixel



Faster data transfer (data sparsification or compression)



# New devices are coming:

# Medipix3 and Timepix2 concept

FNAL, 26th September 2008

Jan Jakůbek


# Medipix3

Two configurable counters per pixel.

Charge summing scheme improves spatial resolution, noise and spectrometric properties.

Two modes of sensor bonding (either 55 x 55 or 110 x 110 um). When larger pixels are connected then they can use all circuitry => 8 thresholds and 8 counters.

#### Medipix3 – charge summing concept







# **Timepix2 concept**

#### Not decided yet !

#### **Possible ways:**

- Two configurable counters per pixel enabling parallel energy and time determination
- Self triggering FAST OR logic
- Fast reset
- Sparse data readout
- Improved preamplifier (noise)

And many other possible requirements ....



## Conclusions

In the field of imaging there are two main directions:

- More sophisticated data processing on the pixel level.
- Application of tracking approach for imaging providing as complex information about each event as possible (Even charge sharing effect can be exploited) => request of very high data throughput.

Steady development in the field of sensors is required.



# Thanks for your attention



#### Charge sharing effect: **Tracks of MIP particles**



- Ionization by MIP particles doesn't depend on depth and follows Landau distribution
- Charge sharing effect is more significant if charge is generated near the surface
- => Charge sharing brings more information in tracking mode

and Applied Physics



#### Charge sharing effect:

### **Tracks of MIP particles – Cosmics**



FNAL, 26th September 2008

Jan Jakůbek



## **Triggered image integration**



#### Coincident imaging: Coincident imaging with Pixel device

Institute of Experimental and Applied Physics Czech Technical University in Prague



#### **Application field:**

- Imaging in Activation Analysis
  - Prompt gamma imaging

#### Activation analysis:

- Excited nucleus emits radiation
- Energy of emitted gamma is typical for each element => direct measurement of element concentration
- Very sensitive method (<ppm)</li>
- To improve selectivity several detectors can be used in coincidence
- Electrons are often present deexcitation in cascades
  - => Chance for thin Si pixel detector<sub>CTU Prague 81</sub>



### Coincident imaging: Sample used for experiment



### Coincident imaging: Results



#### Non coincidence mode

#### **Coincidence mode**



Exposure time was in both cases 1 minute. All dots clearly resolved.

FNAL, 26th September 2008

Jan Jakůbek



### **Enhanced compton camera**

### ... coincidence + energy

FNAL, 26th September 2008

Jan Jakůbek



## **Compton camera enhancement**





## Efficiency



Detector geometry: 15 x 15 x 15 mm of sensitive material

FNAL, 26th September 2008

Jan Jakůbek



# **Simulations of real geometry**

and Applied Physics

Institute of Experimental





## Simulated images of point source

Institute of Experimental and Applied Physics Czech Technical University in Prague



Jan Jakůbek