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Real-time in-vivo μ-imaging with Medipix2

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ABSTRACT

An X-ray micro-radiographic system based on the Medipix2 semiconductor pixel detector for dynamic high spatial resolution and for high contrast imaging has been developed. Our system is based on a micro-focus and nano-focus X-ray tube and the hybrid single-photon counting silicon pixel detector Medipix2 (matrix 256×256 sq. pixels of 55 μm pitch). This compact table-top system stands promising as a new tool in the field of small animal imaging as well as in the in-vivo observation of dynamic processes inside living organisms. The main advantages of these Medipix2 pixel detectors include: high sensitivity to low-energy X-ray photons; position sensitive and noiseless single-photon detection with preselected photon energies; single-quantum counting in each pixel performed by digital counter (therefore there is no dark current); digital integration (providing unlimited dynamic range and absolute linearity in device response to number of photons, high sensitivity and high contrast); real-time digital information, high-speed digital communication and data transfer. We improve the picture quality with the help of statistical data analysis and extended the calibration of individual pixels response. 2D and 3D radiographic images of samples demonstrate the potential and applicability of our system for precise in-vivo X-ray high-resolution dynamic diagnostic and biological studies. Obtained results are shown on small animal and organic samples.

1. Introduction

We present our table experimental setup devoted to a digital high-resolution X-ray transmission in-vivo imaging [1] that was applied to μ-radiography and μ-tomography of small organisms. This setup was designed for X-ray imaging as well as for the observation of real-time in-vivo processes in living organisms [2]. The single-photon counting pixel device Medipix2[1] was used as an image area. Hamamatsu μ-focus X-ray tube or FeinFocus micro-focus or nano-focus X-ray tube was used as X-ray sources.

X-ray imaging of biological samples consisting of soft tissues is particularly difficult due to low differences in beam attenuation. This difficulty can be overcome by using highly sensitive and broad (unlimited) dynamic range images hybrid semiconductor pixel detectors like Medipix2 [3]. In combination with state-of-the-art point like X-ray sources and advanced data imaging analysis it is possible to refine spatial resolution of the system below 1 μm. The capability of the system assembled is demonstrated below on small animal samples.

1.1. The X-ray μ- and nano-imaging system

The system we used (Fig. 1) contained a μ-focus Hamamatsu X-ray tube operated at 40–90 kV and 100–240 μA with spot size 5 μm or FeinFocus FXE-160.51, spot <1 μm operated at 10–200 kV and 50 μA–1 mA (both tubes with tungsten anode), a sample holder (enabling three-dimensional translation and rotation) and the pixel detector Medipix2. The main advantages of the Medipix2 pixel detector include: high sensitivity to low-energy X-ray photons; position sensitive and noiseless single-photon detection with preselected photon energies; photon counting[2] in each pixel performed by digital counter (therefore there is no dark current); digital integration (providing unlimited dynamic range and absolute linearity in device response to number of photons); high-speed digital communication and data transfer.

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[1] See also www.cern.ch/medipix and www.utef.cvut.cz/medipix.

[2] In contrast, change-integrating devices, such as CCDs, show dark current (noise), limited range and non-linear response.

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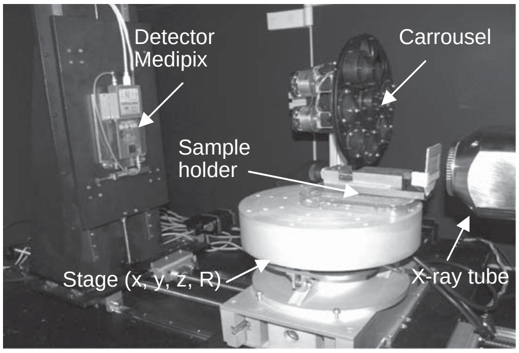

Fig. 1. An experimental setup for X-ray μ- and nano-radiography and μ- and nano-tomography: μ- and nano-focus X-ray tube, sample holder, calibration carrousel and detector.

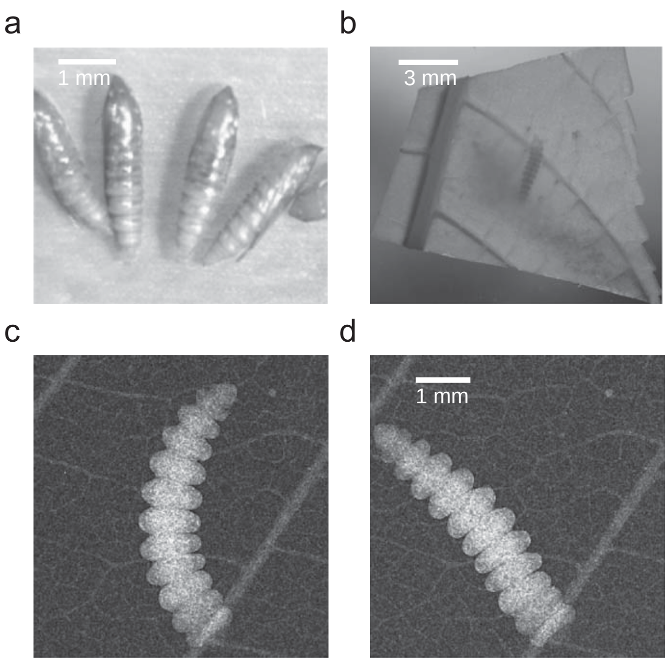

Fig. 2. (a) Photography of a living pupae of leaf miner; (b) Infrared photography of a leaf miner inside a leaf; (c) and (d) Sequence of X-ray μ-images of living larva inside a leaf.

The response of each individual detector pixel was calibrated for different absorber thicknesses to suppress the beam hardening effect in the given object and to compensate pixel inhomogeneity across the whole pixellated sensor [4]. A set of perfectly flat aluminium foils of various thicknesses ranging from 50 to 500 μm was used for calibration. By altering the distance between the sample and the detector, an additional (geometric) magnification from 1 × to 30 × could be set.

2. Living biological samples used for imaging

The X-ray μ-radiography system can be significantly exploited for μ-imaging of soft tissue and be a subject of in-vivo biological studies.

2.1. In-vivo μ-imaging of horse chestnut living larva inside a leaf

The transmission image of a living larva (about 1.5 mm across) is shown in Fig. 2 as a subject of in-vivo biological studies [5,6].

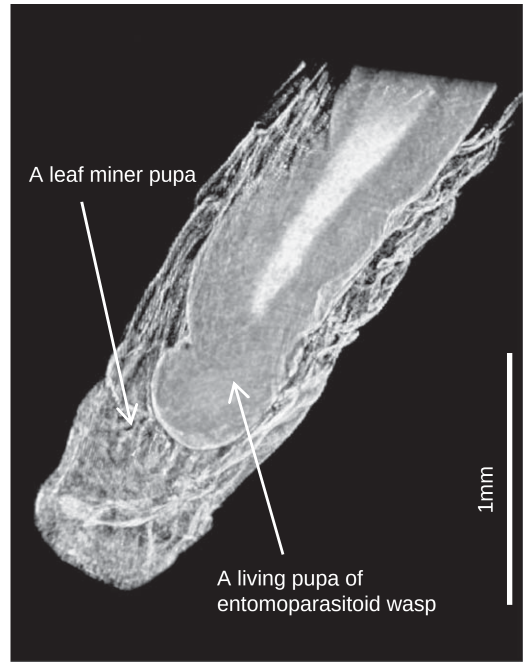

Fig. 3. μ-tomograph of a living pupa of entomoparasitoid inside a leaf miner pupa. The 3D image is computed from 180 projections (5 s each).

The exposure time is 500 ms per frame. Such frames (about 300) can be used for real-time video.

2.2. In-vivo μ-tomography of a living pupa of entomoparasitoid inside a leaf miner pupa

By scanning the sample at several angles and by suitable image reconstruction, high-resolution tomographic images can be obtained with real micrometer-scale resolution. Pictures of entomoparasitoid inside a pupa are shown in Fig. 3 for demonstration. The high dynamic range of detector Medipix2 is proven.

3. Conclusion

Detector Medipix2 is suitable for imaging of biological samples as it was shown. Detector enables in-vivo and dynamic real-time imaging. It brings single-quantum and real-time digital information about studied objects with high resolution, high sensitivity and broad dynamic range. Medipix2 is suitable for real-time imaging due to fast hardware properties, which are limited by power of X-ray tube. These types of detectors open new possibilities for researchers to perform non-invasive high-resolution studies of living objects and tissues [7,8].

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