

## Replaceable Microfluidic Cartridges for a PCR Biosensor

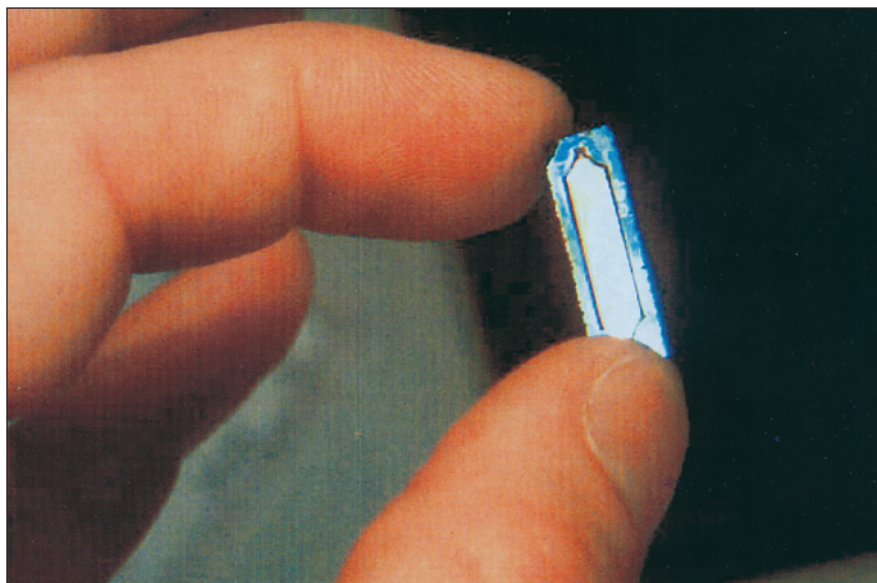
Design has been optimized for detection of target DNA sequences.

Lyndon B. Johnson Space Center, Houston, Texas

The figure depicts a replaceable microfluidic cartridge that is a component of a miniature biosensor that detects target deoxyribonucleic acid (DNA) sequences. The biosensor utilizes (1) polymerase chain reactions (PCRs) to multiply the amount of DNA to be detected, (2) fluorogenic polynucleotide probe chemicals for labeling the target DNA sequences, and (3) a high-sensitivity epifluorescence-detection optoelectronic subsystem.

Microfluidics is a relatively new field of device development in which one applies techniques for fabricating microelectromechanical systems (MEMS) to miniature systems for containing and/or moving fluids. Typically, microfluidic devices are microfabricated, variously, from silicon or polymers. The development of microfluidic devices for applications that involve PCR and fluorescence-based detection of PCR products poses special challenges:

- Biocompatibility of materials is a major requirement. Contact of DNA-containing fluid specimens with silicon inhibits PCR. It is necessary to either fabricate a PCR microfluidic device from a suitable polymer or else micromachine the device from silicon and coat its interior surfaces with a suitable polymer.
- Recently developed polymeric materials from which other biocompatible microfluidic devices are made do not have the high thermal conductivity and low heat capacity needed to facilitate the rapid thermal cycling that is essential for efficient PCR.
- It is difficult to integrate spectroscopic windows into microfluidic devices. Thermal-expansion mismatches between silicon substrates and glass windows lead to failures of devices.
- Multiple passes of an excitation light



This **Microfluidic Cartridge** is a micromachined device that contains fluid specimens during PCR cycles and serves as an optical cell for detection of fluorogenically labeled DNA sequences.

beam are needed to obtain adequate sensitivity for detection; this need further complicates the problems of design and fabrication.

The design and fabrication of the replaceable microfluidic cartridges meets these challenges. The cartridges are made from a combination of materials, based on micromachined silicon substrates. The thermal-expansion-mismatch problem was solved by use of thick (3 mm) silicon substrates and anodically bonded thick (0.7 mm) covers made of borosilicate float glass. The fluorescence signal is enhanced by use of multipass optics, an essential component of which is a reflective film of chemical-vapor-deposited aluminum on a square glass plate affixed to the bottom of the cartridge by use of epoxy. The in-

terior surfaces of the fluidic channels are coated with dodecyltriethoxysilane.

The design of the cartridge has been optimized along with that of the rest of the biosensor for detection of target DNA in a microgravitational or normal gravitational setting. In a test, the biosensor was found to be capable of reliably detecting 600,000 copies of the human  $\beta$ -actin gene after as few as five PCR cycles.

*This work was done by Kevin Francis and Ron Sullivan of Systems and Processes Engineering Corp. for Johnson Space Center. For further information, contact:*

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## CdZnTe Image Detectors for Hard-X-Ray Telescopes

Image sensors are designed for high spectral resolution and low power consumption.

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Arrays of CdZnTe photodetectors and associated electronic circuitry have been built and tested in a continuing effort to develop focal-plane image sensor systems for hard-x-ray telescopes. Each

array contains 24 by 44 pixels at a pitch of 498  $\mu\text{m}$ . The detector designs are optimized to obtain low power demand with high spectral resolution in the photon-energy range of 5 to 100 keV.

More precisely, each detector array is a hybrid of a CdZnTe photodetector array and an application-specific integrated circuit (ASIC) containing an array of amplifiers in the same pixel pattern as that

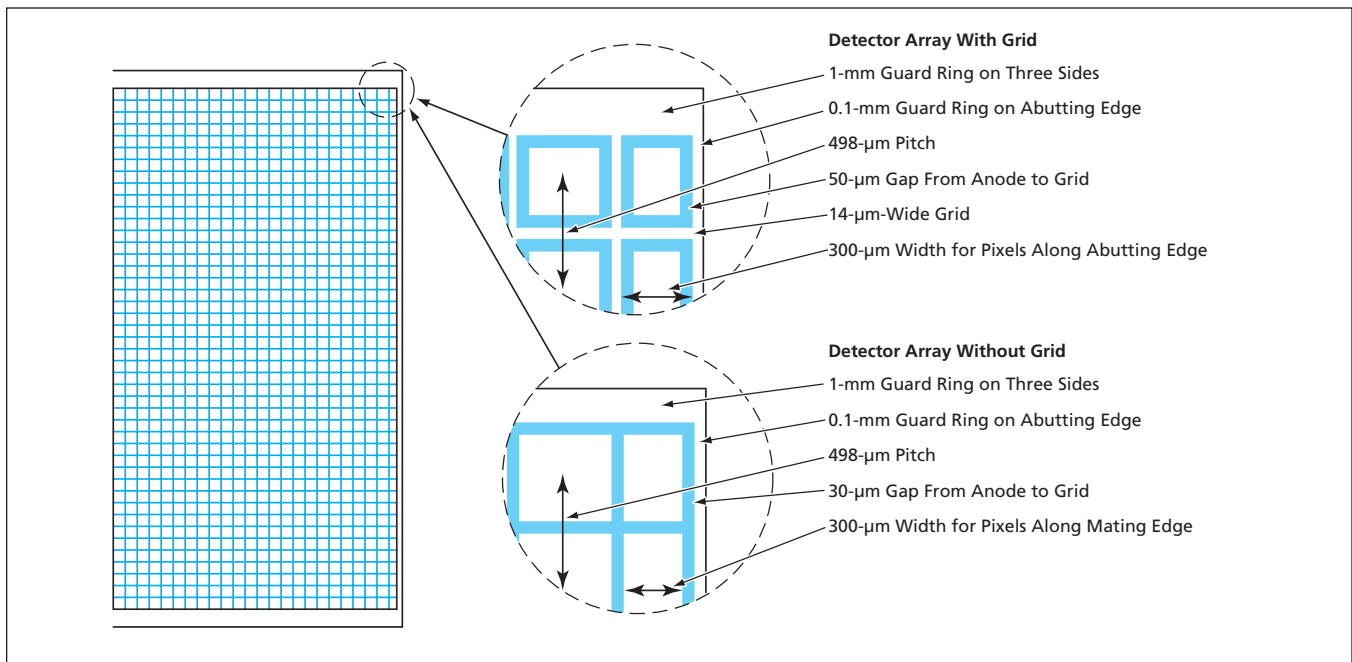


Figure 1. Two Different Anode Patterns have been evaluated: one for a detector array with and one for a detector array without a shaping grid.

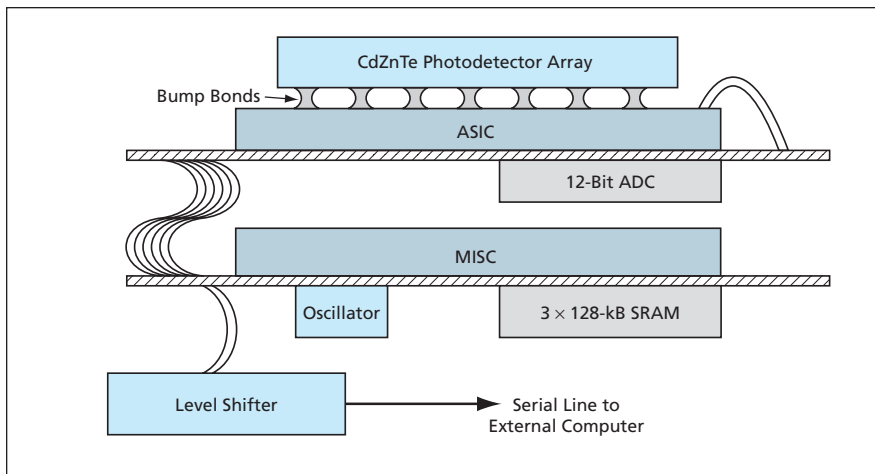


Figure 2. An X-Ray Image Sensor System is based on a hybrid of a CdZnTe photodetector array with an ASIC containing an array of amplifier circuits.

of the detectors. The array is fabricated on a single crystal of CdZnTe having dimensions of 23.6 by 12.9 by 2 mm. The detector-array cathode is a monolithic platinum contact. On the anode plane, the contact metal is patterned into the aforementioned pixel array, surrounded by a guard ring that is 1 mm wide on three sides and is 0.1 mm wide on the fourth side so that two such detector arrays can be placed side-by-side to form a roughly square sensor area with minimal dead area between them.

Figure 1 shows two anode patterns. One pattern features larger pixel anode contacts, with a 30- $\mu\text{m}$  gap between them. The other pattern features smaller pixel anode contacts plus a contact for a shaping electrode in the form of a grid

that separates all the pixels. In operation, the grid is held at a potential intermediate between the cathode and anode potentials to steer electric charges toward the anode in order to reduce the loss of charges in the inter-anode gaps.

The CdZnTe photodetector array is mechanically and electrically connected to the ASIC (see Figure 2), either by use of indium bump bonds or by use of conductive epoxy bumps on the CdZnTe array joined to gold bumps on the ASIC. Hence, the output of each pixel detector is fed to its own amplifier chain.

In the ASIC, each pixel contains a pre-amplifier, a shaping amplifier, a discriminator, and sampling and pulsing circuits. All the pixels share a serial readout line. The ASIC has been designed to op-

erate with low noise and to consume no more than about 50 mW of power in normal operation.

The ASIC is controlled by a micro-processor — a 24-bit minimum-instruction-set computer (MISC) implemented on a field-programmable gate array. The MISC runs on a 7.3728-MHz clock cycle that is established by an oscillator that runs at a frequency of 14.7456-MHz. Three static random-access memory (SRAM) circuits provide a total of 128 kB of 24-bit memory. The output of the ASIC readout line is fed to a 12-bit analog-to-digital converter (ADC) that consumes 80 mW of power. The MISC then feeds the output of the ADC to a level shifter that, in turn, transmits the digital output to an external computer via a serial data line.

The sensor system consumes 700 mW of power. By careful design of the ASIC and off-chip digital signal processing, it has been possible to achieve energy resolution less than 1 keV for hard x-rays at an operating temperature of 0 °C.

*This work was done by C. M. Hubert Chen, Walter R. Cook, Fiona A. Harrison, Jiao Y. Y. Lin, Peter H. Mao, and Stephen M. Schindler of the California Institute of Technology for Goddard Space Flight Center. Further information is contained in a TSP (see page 1).*

*This invention is owned by NASA, and a patent application has been filed. Inquiries concerning nonexclusive or exclusive license for its commercial development should be addressed to the Patent Counsel, Goddard Space Flight Center, (301) 286-7351. Refer to GSC-14804-1.*