LETTER

A novel CIS pixel structure design and simulation for DNA fluorescence sequencing

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Abstract Miniaturization of DNA fluorescence sequencing is important to reduce costs and promote audiences. Among them, CMOS image sensor (CIS) is an effective method for fluorescence detection. In order to solve the problems of large pixel area and low throughput in CIS chip sequencing technology, we have designed a new CIS pixel structure with special hexagonal topology, reduced floating diffusion (FD) capacitance, improved conversion gain, and applied neighborhood-dark-current-cancellation technology. Simulations using sentaurus and numerical FDTD software show that the capacitance of FD node is 0.48F and 0.496F for different PDS respectively, meaning the whole conversion gain is about 320 μV/c- before the back-end process. The relationship between the sensitivity efficiency of hexagon pixel structure and the edge length of the photodiode (PD) shape and the micro lens (ML) shape was investigated. The optimal design conditions were determined, that is, 1.8 um hexagon PD edge length, or 1.6 um octagon PD edge length, with 2.3 um ML thickness and 2.5 um curvature radius.

key words: CMOS image sensor, pixel layout, floating diffusion, conversion gain, microlens

Classification: Integrated circuits

1. Introduction

With the development of biomedical technology, DNA sequencing is playing an increasingly important role, which can be widely used in disease diagnosis, antenatal examination of pregnant women and biological identification. The continuous development of DNA sequencing technology, including the second generation and third generation technology (pyrosequencing [1], Solexa [2], SOLID [3], ZMW [4, 5], Nanopore [6, 7], etc.) has been widely used in biological industry and scientific research. However, there are still some problems, such as large volume of device, low throughput and high cost. Therefore, CIS chips with CMOS technology have been widely concerned.

Many research has been conducted on the application of CIS in DNA sequencing [8-16]. B. Jang et al [17, 18, 19, 20] proposed a CIS based biosensor, with the application of optical fiber panel (FOF) to connect the biological reaction layer and the photosensitive layer to prevent scattering, maintain the light intensity and reduce the crosstalk. H. Eltoukhy et al [21, 22, 23] adopted low dark current PD, low noise differential circuit, correlation coupling sampling, multiple digital averaging method and noise reduction technology to improve the sensitivity under low brightness for bioluminescence detection. S. Parikh et al [24, 25, 26] detects DNA in microarrays with CIS by improving mechanical alignment, laser source noise, circuit noise, and conversion gain. The differential output is used to satisfy the differential input requirement of the counting circuit, while reducing the sensitivity to common mode and power noise. A. Manickam et al [27, 28, 29, 30] presents an integrated biochip with a specific DNA probe sequence in each biosensing unit, a wavelength-selective multimedia emission filter, and a high-performance programmable photoelectric detector for a resistance heater. Biochemical reactions occur on the surface of the photosensitive area, which enables continuous wave fluorescence detection to improve the dynamic range and reduce the noise. However, they still have some problems, such as over large pixel area, low effective throughput, single application scenario and so on. In response to this situation, we propose a special pixel design for fluorescence signal detection, which can meet the high-throughput and low-intensity photosensitivity requirements for single-molecule DNA fluorescence sequencing and can be adapted to a variety of scenarios.

The innovations of this article include:

1) Hexagonal layout structure, which can be matched with optical panel to achieve the matching with a variety of different sizes and functions of microfluidic structures.

2) Floating diffusion (FD) capacitance reduction, achieving optimization of FD nodes, reduction of capacitance and improvement of conversion gain (CG) through particular layout design, including AA zone optimization and metal alignment adjustment.

3) Differential dark current cancellation, using redundant pixels for adjacent dark current cancellation to
minimize dark current noise.

2. Method

In order to match the optical panel, reduce the loss of light intensity during transmission and suppress crosstalk, a hexagonal honeycomb pixel layout is designed. The gate of transistors are connected with wires in metal2 layer in the horizontal direction to load drive signals, and the VDD and output voltage signal are transmitted vertically by using wires in metal 3 layer to bypass the PD area of the pixel. As the first-stage input transistor, the source follower (SF) is placed away from the wires to transmit driving signal and covered with metal shield in metal3 layer, which reduces the influence of thermal noise, varying voltage, and the impact of incoming light.

When using a hexagonal layout structure, the staggered arrangement of pixels makes it difficult for metal wires to avoid sheltering the photodiode area. In addition, since a single pixel corresponds to a separate DNA chamber, crosstalk between different chambers needs to be excluded. In order to reduce the impact, the area of the PD is reduced and the shape (hexagon or octagon) is adjusted under the premise of ensuring the photosensitive efficiency, while the influence from the area of the PD shape used and parameter of micro lens (ML) is analyzed.

By modifying the connection location between the transfer transistor (TX) and FD, that is, by arranging the gate of the TX from the side of the polygon PD and reducing the distance from the gate of the dual-conversion-gain (DCG) transistor at the FD source to the TX gate end, the FD area and perimeter can be reduced while ensuring the smooth transfer of electrons from the PD. And reduce the distance between FD node and active area (AA) zone of SF transistor, and optimize the metal path between FD and SF transistor to reduce the length of wire in metal1 layer. These measures can reduce FD capacitance and improve CG.

Based on the above considerations, two pixel layouts with different PD structures are designed, as shown in Fig.1. (hexagonal PD) and Fig.2. (Octagonal PD).

To assess and reduce the effects of pixel crosstalk and dark current, neighborhood-dark-current-cancellation technology is illustrated, which means some pixels are set to be insensitive and unresponsive, that is, as shown in Fig.3., at six adjacent pixel locations around a valid pixel photosensitive point corresponding to a microfluidic micro-chamber, the photosensitive
capability is preserved at the left and right adjacent locations but not corresponding to the micro-chamber, which is used to detect and filter the optical crosstalk of adjacent pixels. In the upper left, upper right, lower left, and lower right neighborhoods, a metal barrier is used to block the sensitivity and to eliminate dark currents at the output. These measures can effectively reduce dark current and crosstalk effects. Although this method will cause the decrease of valid sensing resolution, it can still meet the requirement of one-to-one coupling with the reaction location considering the relative large size and interval of micro chamber.

3. Simulation results and discussion

3.1 Pixel optical simulation
In order to confirm the photosensitivity performance of our pixel structure and determine the optimal parameters, optical simulation on pixel structure with both hexagon PD and octagon PD is conducted. Lumerical FDTD software is used to simulate the light absorption rate. Vertical shape structure (a hollow regular hexagonal metal plate with an edge length of 3um was used to simulate the pixel sensitive boundary) and corresponding materials were built, and the incident light (wavelength between 500nm and 550nm, near the wavelength of fluorescence signal induced by FAM, which is 542nm) and the light detection were added to simulate the correlation between the edge length and light absorbance of hexagonal and octagonal PD, respectively. Fig.4 shows the appearance of the simulation structure and Table 1 shows the material type and thickness of the structure. As a result shown in Fig.5, the absorption efficiency decreases as the area of the PD used decreases. When the PD area is similar, the light absorption of hexagonal PD, due to the more likeness to pixel shape, is slightly higher than that of octagonal PD. For practical use, when the pixel size is a hexagon with area of about 23.4 um² (side length is 3 um), a hexagonal PD with area of about 8.42 um² (side length of 1.8 um) or an octagonal PD with area of 8.96 um² (side length of 1.6 um) can achieve more than 85% light absorption.

![Fig. 4. Pixel structure in optical simulation](image)

**Table 1 Material type and thickness of the simulation structure**

| Materials                               | Thickness (um) |
|-----------------------------------------|----------------|
| Si (PD area)                            | 3              |
| Oxide (isolation above PD)              | 0.03           |
| SiN (isolation above PD)                | 0.045          |
| Oxide (isolation for Poly and metal)    | 2.455          |
| SiN (isolation under colorfilter)       | 0.146          |
| Colorfilter                             | 0.75           |
| Microlens                               | 1.4            |

![Fig. 5. Absorption rate vs PD side length @ different PDs](image)

Moreover, based on the same vertical structure, the morphology and size of the surface micro lens are adjusted, and the correlation between the parameters of the micro lens and the light absorption efficiency is simulated. The results are shown in figure. 6. When the radius of ML curvature is fixed, the thickness of ML is closer to the radius of curvature, the absorption
efficiency of PD is higher. And if the thickness of ML is slightly smaller than the radius of ML curvature, the absorption efficiency decreases slightly, but when the thickness of ML is larger than the curvature radius, the absorption efficiency decreases significantly. When the thickness of ML is fixed, the larger the radius of curvature, the more efficient the absorption of PD. Considering the limitation of pixel size (radius of tangent circle of hexagon with 3um edge length is 2.6um), the structure parameter of ML is set as curvature radius 2.5um, thickness 2.3um.

4.2 Pixel FD capacitance simulation
The circuit design was carried out under the Dongbu 0.11um 1P3M process, the pixel layout for both hexagon PD structure and octagon PD structure are shown in Fig.7, which is similar as the appearance in Fig.1. and Fig.2. The PD is covered by metal lines only at the corner or edge on which little light incident, so the photosensitive efficiency is little affected. The peripheral circuit consist of row-decoder, column readout circuit with single-slope analog-digital converter (ADC), digital core and so on. To analyze the CG, the FD capacitance is simulated by sentaurus, and the result is shown in Fig.8.
Continuous base identification for single A CMOS Image Sensor Utilizing Opacity of... quality control for... (JCYJ201... technology,”... sequencing... fluorescence signals, and can even achieve detection capabilities close to single molecules. The simulation results verify the rationality of the design and clarify the specific parameters of the design, such as FD node capacitance, PD size and shape, ML morphology and size. In the future, chip projection will be based on these parameters, functional testing and data analysis of the packaged chip will also be carried out.

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Fig. 8. The simulation on FD capacitance of pixel with (a) hexagon PD and (b) octagon PD

From top to bottom, figure 8 shows the simulation top view, the simulation cross-section view and curve of FD electrons vs voltage for both PD structures. The FD capacitance for hexagon PD structure and octagon PD structure is 0.48fF and 0.498fF respectively after calculation on slopes. And the conversion gain could be easily calculated, which are 333 uV/e- and 321 uV/e- respectively before the back-end process. Considering the particular design on the decrease of connected metal length between FD and SF gate, the increased capacitance of FD after back-end process could be limited to 30% due to previous experience. So the total CG could be a large value more than 250 uV/e-, which is a high level to meet our requirement. With the high CG, the column readout circuit could output effectively with fewer electrons, which leads to a smaller minimum light sensitivity and a higher SNR. Moreover, the fluorescence signal intensity needed to each pixel could decrease, meaning the less need DNA fragment and high accuracy on sequencing.

4. Conclusion

By applying special hexagonal pixel structure, reducing FD capacitance to improve conversion gain, and using neighborhood-dark-current-cancellation technology, CIS chips can be more ideal for detection of DNA fluorescence signals, and can even achieve detection capabilities close to single molecules. The simulation results verify the rationality of the design and clarify the specific parameters of the design, such as FD node capacitance, PD size and shape, ML morphology and size. In the future, chip projection will be based on these parameters, functional testing and data analysis of the packaged chip will also be carried out.

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