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Wireless capsule for autofluorescence detection

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Abstract

Variations in tissue autofluorescence (AF) can be exploited to detect early signs of intestinal cancer, however current endoscopic AF systems are only able to inspect the oesophegus and large intestine. We present the design, fabrication and testing of a pill capable of inducing and detecting AF from mammalian intestinal tissue. The prototype comprises an application specific integrated circuit (ASIC), illumination LED, optical filters to minimize sensor response to crosstalk from the illumination wavelength, a pulse counter/control unit and a radio transmitter. The ASIC contains a single photon avalanche diode detector (SPAD), and integrate high voltage charge pump (up to 37.9V) power supply. The SPAD operates above its breakdown voltage to operate in Geiger mode, and exhibits a detection efficiency peak at 465 nm, sufficiently close to human tissue autofluorescence's peak of 520±10nm. The ASIC was fabricated using a commercial high-voltage CMOS process. The complete device uses only 21.4 mW.

Keywords: Autofluorescence endoscopy, endoscopic capsule, SPAD, non-invasive diagnosis

1. Introduction

Currently available technology allows the oesophagus and colon to be inspected visually via endoscopy, and the entire gastro-intestinal tract to be similarly examined by capsule-based camera sensors [1-2]. However signs of disease, particularly early stage cancer, may be missed in viewing the 7-9 hours of images generated [4]. Autofluorescence imaging (AFI) exploits the fact that cancerous intestinal tissue exhibits a considerably lower autofluorescent response than healthy tissue when excited by blue or UV

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light, and offers improved prospects for cancer detection compared to white-light inspection [5, 6]. A commercial AFI system [6] is endoscope-based (and hence unable to access the small intestine). This work implements a wireless capsule-based system which can be used to detect autofluorescence variations in the small intestine.
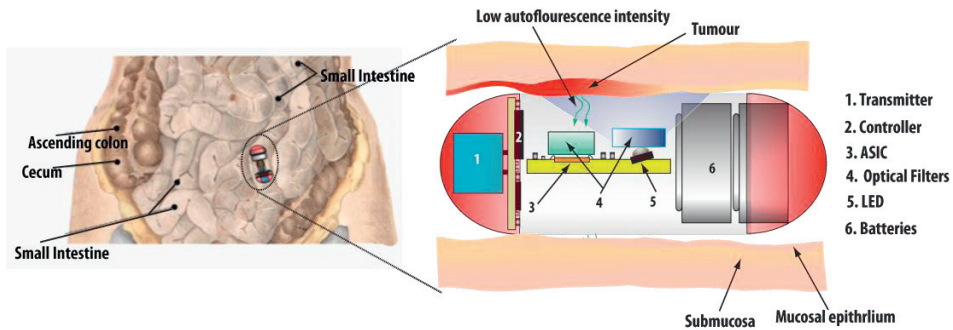

Fig. 1 Concept of examining the small intestine using pill for detecting autofluorescence.
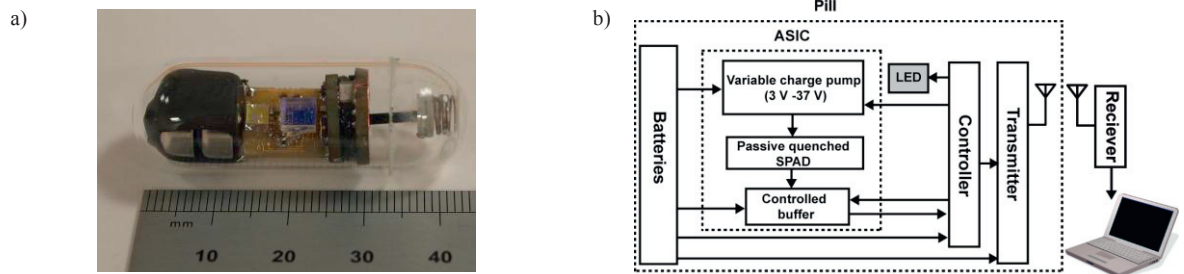

Fig. 2.   a) Packaged pill. From left to right: battery pack, LED and ASIC on a horizontal PCB, vertical controller and transmitter PCBs, and UHF antenna.   b)   Complete system block diagram illustrating the components of the pill and the radio link to the external base station.

2. System Description

The capsule sensor (Fig. 2.a) utilises an LED to illuminate intestinal tissue at a wavelength of 465 nm. Tissue autofluoresces in response at 520 nm, generating photons which impact on the active area of a Single Photon Avalanche Diode. A bandpass filter with 475nm centre wavelength on the LED and a long-pass filter with 515nm cutoff over the SPAD light detector prevent illuminating photons from the LED from triggering the SPAD. A series of charge pumps generate the 37.9V SPAD bias voltage from the 3V onboard battery supply. The SPAD pulse output drives a comparator/buffer readout circuit. This in turn feeds a counter, which counts the number of photons received over a 500 ms period. This value is read once per second by a state machine controller, and transmitted via a UHF radio link. This is picked up by an external radio receiver and microcontroller, and passed to a PC via USB for logging and analysis (Fig.2.b). The charge pump, SPAD and readout circuit are integrated onto an unmodified commercial 0.35µ 4-metal high voltage triple-well CMOS-process ASIC, triple-well process minimising current leakage which is generated due to the clocking nature of the charge pumps.

The SPAD is reverse-biased by the charge pump to in excess of its breakdown voltage (Fig. 3.a). The charge pump is derived by a 3V-clock at 10.922kHz which is supplied externally by the controller. A

photon emitted by intestinal autofluorescence striking the active area initiates an avalanche breakdown, causing a substantial increase in current flow due to discharge of the p-n junction's capacitance and a drop in SPAD voltage. This leads to a voltage pulse at the SPAD anode which is detected and buffered by comparator M1/M2 and inverting buffer M3/M4. Current sink Mq limits the SPAD recharge rate and therefore decreases the generated pulse width and increasing dynamic range.

Fig. 3. a) SPAD and passive quenching circuit. b) Pulse Counter and UHF Data Link. The counter counts pulses over 500ms in every second. The counter value is read serially and transmitted to an external logger via UHF radio. A divider generates counter gate control and charge pump clock signals.

Pulses from the SPAD increment a free-running counter which rolls back to zero on reaching its maximum value of 2^{24}-1 [8]. The counter input gate opens for 500ms per second. At the end of the sampling period the control state machine transmits the counter value at 32.768 kbaud via an amplitude-shift-keyed transmitter and omnidirectional helical antenna. The 868.3MHz radio frequency is licence-exempt and within the 450-900 MHz range shown to be effective for transmission through the human body [7]. The external receiver passes the incoming data packet via a USB microcontroller to a PC, which calculates pulse rate per second from the 2 most recent count values. A Xilinx Complex Programmable Logic Device (CPLD) implements the counter, multiplexer and control state machine and divides the 32.768KHz system clock by 3 to generate the 10.922kHz charge pump control clock frequency, f_c, and by 215 to produce a 1Hz, 50% duty cycle counter gate control signal.

The prototype is packaged in a glass tube of borosilicate glass which has a visible light transmission >92%. The design included the following components: an 11mm x10mm double-sided PCB board for the ASIC, LED, optical filters and charge pump capacitors; a double-sided 12mm diameter round PCB implementing the counter and control unit and a double-sided 14 mm diameter round transmitter PCB; two SR48 batteries. The complete prototype (Fig. 2.a) is 16mm x 45mm in size and weighs 12g including batteries.

3. Experimental Evaluation

We tested our device's ability to induce tissue autofluorescence, and to differentiate autofluorescence from additive noise in the form of dark count, crosstalk between the LED and the SPAD, and back-scatter from the blue excitation illumination. Direct illumination of the SPAD by the LED (Figs.4. a,c) produced a photon count of c. 89kcps. This rose to over 737 kcps when lamb intestine was placed between the LED and SPAD. When the LED and SPAD were installed side by side to test reflection performance (Figs.4. b, d), the SPAD generated a dark count rate of c. 4kcps in complete darkness. With the excitation LED on, the count rate rose to c. 8.9kcps. A reflective foil sample positioned at a distance of 1.5cm resulted in a

pulse count of c. 37 kcps. Replacing the foil with lamb intestine caused the pulse count to rise to 83kcps. The photon counts obtained from intestinal tissue are clearly substantially in excess of those from backscatter and crosstalk, demonstrating that the system is capable of inducing tissue autofluorescence which is clearly detectable in spite of these additive noise sources.
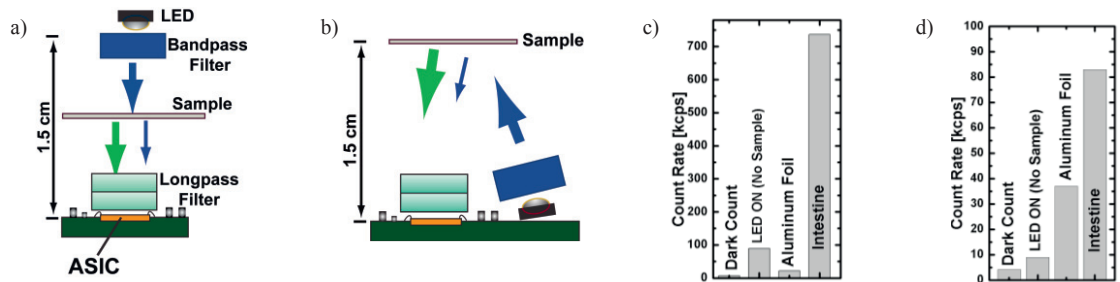

Fig 4: a) Direct illumination autofluorescence measurement setup. b) reflection measurement setup. c) direct illumination results. d) reflection results. The response from intestine substantially exceeds reflection, dark count and crosstalk, clearly demonstrate the ability to induce and detect autofluorescence in lamb small intestinal tissue.

4. Conclusion

Our work demonstrates the feasibility of a capsule sensor system capable of autofluorescence-based inspection of the entire gastrointestinal tract. The scalable technology used brings us closer to development of a Wireless Autofluorescence Video Endoscope (WAVE).

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