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A low-cost, linear, DC – 35 MHz, high-power LED driver for continuous wave (CW) and fluorescence lifetime imaging (FLIM)

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Abstract

Near-infrared (NIR) fluorescence has the potential to provide surgeons with real-time intraoperative image-guidance. Increasing the signal-to-background ratio of fluorescent agents involves delivering a controllable excitation fluence rate of proper wavelength and/or using complementary imaging techniques such as FLIM. In this study we describe a low-cost linear driver circuit capable of driving Light Emitting Diodes (LEDs) from DC to 35 MHz, at high power, and which permit fluorescence CW and lifetime measurements. The electronic circuit Gerber files described in this article and the list of components are available online at www.frangionilab.org.

Keywords

LED driver; intraoperative imaging; optical; low-cost; fluorescence; FLIM

1. INTRODUCTION

Recent progress in biomedical optical imaging shows great potential for real-time *in vivo* applications. In particular, fluorescence imaging has proven potential to provide surgeons with faster and more precise information during surgery.^{1,2,3,4,5} For instance, the use of FDA-approved fluorescent tracers for sentinel lymph-node mapping shows significant advantages compared to the blue-dye.³ It provides faster and more accurate localization of nodes that can improve the quality and reduce the amount of time of the current procedure. Many other applications could benefit from the flexibility of real-time fluorescence imaging. In particular the development of fluorescent targeted ligand such as breast micro-calcifications⁶ and prostate specific membrane antigen (PSMA)⁷ could greatly improve cancer detection and resection.

Consequently it is necessary to develop tools for imaging fluorescence in real time and *in vivo*.^{8,9} The excitation light source requires particular attention as it needs to be high enough for exciting the fluorophore to a detectable level. Proper filtration of excitation and emission as well as fluence rate control is also crucial for obtaining the desired fluorescence information. However, this imaging technique meets limitations when undesired light is collected through the fluorescence channel. Possible sources of noise are inadequate optical filtration, auto-fluorescence or exogenous and endogenous fluorophores present in the sample of interest. Several approaches are possible for identifying these sources of noise. One can take advantage of their spectral signature, their quantum yield, if any, and their time-related characteristics.¹⁰

LEDs appear to be an attractive solution for a surgical light source for surgery because they are safe, inexpensive, powerful, can be modulated in intensity, and available at many wavelengths. Unfortunately there are currently no commercially available, high-frequency, linear LED drivers. In order to control the fluence rate of the excitation light and investigate noise rejection capabilities, we developed a compact, low-cost, and linear LED driver. This driver can control LEDs intensity by linearly setting the current proportional to an input control voltage. We used this circuit to drive near-infrared (NIR) LEDs (L760-AU from Epitex, Japan) from DC to 35 MHz under recommended and maximum conditions to a maximum filtered power of 100 mW. We validated the Fluorescence Lifetime Imaging (FLIM) capabilities of this driver by comparing it to a laser diode.

2. LED DRIVER

2.1. General description

Driving LEDs requires controlling the amount of current that is flowing in them while providing the proper forward voltage to open the diode. The best known circuit for driving an LED is obtained by inserting a resistor in series and controlling the voltage across both. Current will then be set by Ohm's law across the resistor. In this example, current is set passively through the resistor, and is difficult to control as it is coupled to the forward voltage. More importantly its control is not linear. To solve these issues, one needs some method to decouple the control of the forward voltage and the control of the current flowing through the LED.

We decided to implement a current sink configuration using an operational amplifier (op amp) and a MOSFET transistor.¹¹ Illustrated in Figure 1.A. this configuration consists in controlling a voltage across a sensing resistor isolated from the op amp by the transistor. Current will then be controlled passively through the potential difference upon the sensing resistor. An independent supply voltage ensures the LEDs' forward voltage, which they require to function with the current flow imposed. Linearity of the control is ensured by the feedback loop of the non-inverting circuit.

2.2. Circuit design

The final circuit we designed is illustrated in Figure 1.B. The principle of this circuit is the same as previously described. We added resistors and capacitors for stability purposes as the op amp we chose has high frequency capabilities and thus is very prone to high frequency

oscillations. For instance, capacitors have been inserted to reduce noise on input lines. Also, the resistor to ground at the positive input is there to ensure complete shut off of the LEDs if the control cable is unplugged. Similarly the bias voltage in the negative input of the op amp compensates a high input bias current from the op amp we chose.

Each board is composed of two driving circuits. Each circuit drives 6 LEDs for a total of 12 LEDs. Both circuits share same inputs and ground but are independent from each other. We chose the sensing resistor to be $10\ \Omega$ allowing a 0 – 100 mA current control using a 0 – 1 V input voltage.

3. PARTS AND METHODS

2.1. LED Driver

2.1.1. Parts—The electronic circuit Gerber files described in this article and the list of components are available online at www.frangionilab.org. The driver is composed of simple, available, and inexpensive electronic components. To ensure high frequency capabilities, two components in this circuit are crucial: the op amp and the MOSFET. The op amp we chose is a MAX4451 (Maxim Integrated Products Inc., OR) working in a single supply 0 – 5V configuration, capable of rail-to-rail operation and with a high slew-rate ($485\text{V}/\mu\text{s}$). The MOSFET is a ZETEX ZVN3306F with breakdown drain-source voltage of 60V, 150 mA maximum current, $5\ \Omega$ drain-source resistance and 35pF input capacitance. All capacitors are rated X7R for good frequency behavior. We chose to drive LEDs from Epitex, in particular L760-AU since they are high power (18 mW) and of wavelength of interest of our fluorophores.

Input signal to the circuit has been provided using a dual channel Hewlett-Packard (HP) model HP-3245a for the DC component and Aeroflex IFR2023 for the AC component. Both signals have been combined using a Mini-Circuit bias-tee model ZNBT-60-1W. Power has been supplied by a B&K Precision triple output power supply. One output used was the fixed 5 V and the other was scaled to the forward voltage needed to drive the LEDs (usually 13 V).

All electrical signals have been measured with a LeCroy WaveSurfer 44Xs, 400MHz and 2.5 GS/s oscilloscope. Optical signals have been acquired using a NewFocus 125 MHz ultrafast photodiode model 1801-FS and visualized using the oscilloscope.

2.1.2. Methods—The driver board interconnects a custom-made LED board (Figure 3). Voltages are applied at the board input and the optical output measured with the photodiode. The AC input control voltage has been set at 0 V first and the DC rose to 250 mV. The AC sinewave is then powered on at 500 Hz and increased to 500 mV pp. Resulting voltage at the bias-tee is a 0 to 500 mV sinewave voltage giving a 0 to 50 mA current sinewave in the LEDs. At this frequency the driver drives from ground to 50 mA at full depth of modulation. The photodiode is then placed in front of the LEDs so that its output is modulated from 0 to 1 V. Finally frequency is increased and photodiode output modulation is monitored as an independent control of the driver's optical response.

2.2. FLIM experiments

2.2.1. Parts—The LED driver previously described has been used as a light source in a FLIM setup. For comparison and validation of the driver's FLIM capabilities, we used a laser diode. The laser diode used was a Sharp 120 mW GH0781JA2C. We mounted this diode on a ThorLabs TCLDM9, temperature controlled laser diode mount with an external RF input for modulation. The laser diode intensity has been controlled using a ThorLabs LDC220 and temperature controlled using a ThorLabs TEC200. More information about this diode laser setup is available at www.frangionilab.org. Both light sources share the same AC input from an Aeroflex IFR2023. The driver uses the exact same configuration as described in the section above.

Images have been taken using our regular fluorescence imaging system⁸ but with the addition of a genIII (ITT Night Vision) image intensifier tube (IIT). The image intensifier tube DC voltages are controlled by a custom made GBS power Supply (GBS, San Jose, CA) and inserted in a custom made circuit (GE Global Research, Niskayuna, NY) for noise reduction and allowing high voltage modulation of the photocathode. The IIT multi-channel plate and photocathode DC voltages can be adjusted using 0 – 10 V power supplies. A second Aeroflex IFR signal generator, frequency locked to the first one, has been used in conjunction with an Amplifier Research 25W power amplifier. These two signal generators are capable of generating a 100 V pp sinewave to allow for the modulation of the photocathode. The schematic of the FLIM setup is shown in Figure 2.

Finally a custom made LabView program running on a PC has been designed to automatically phase-shift one signal generator compare to the other, record and quantify images. Data analysis has been performed using Microsoft Excel and GraphPad Prism.

2.2.2. Methods—First, voltages to light source under investigation have been calibrated and optical output checked using the fast photodiode. Second, voltage to the photocathode of the IIT has been checked to be 100 V pp. Third, a well known fluorophore (ICG in DMSO) has been placed on the sample area, the light source DC value turned on, and the IIT power supply powered on. The IIT DC voltages are then setup to visualize the compound with enough signal and without saturating the camera. The AC components of both the light source and the IIT are turned on. Phase is manually shifted to visualize whether the system is working. If the system is working, one should see a periodic increase and decrease with the phase shift. Finally, the samples are placed, acquisition using our custom-made Labview program is run, and images processed. This scheme is repeated for each light source (laser diode and LEDs).

The measurement performed was the relative fluorescence lifetime between 1 μM of ICG in DMSO and 10 μM of ICG in water. Results obtained with the LED driver were compared to the results obtained with the laser diode.

4. RESULTS AND DISCUSSION

4.1. Results

4.1.1. LED driver—Boards were manufactured by Nashua Circuits (Nashua, NH) and assembled by Sure Design (Farmingdale, NJ). Each board measures 25 mm in diameter. Figures 3.A. and 3.B show the top and the bottom of the driver board. Figure 3.C. shows how the driver board and the LED board inter-connect. Finally both boards are molded together using Silicon by Albright Technologies (Leominster, MA) for heat dissipation (Figure 3.D.). At the bottom of the board we added a temperature sensor (Andigilog aTS50) for temperature monitoring.

Figures 4.A and 4.B show optical performance versus frequency of the driver combined with the L760-AU Epitex LEDs under recommended and maximum conditions. Optical output has been scaled to full depth of modulation. Figure 4.A illustrates the optical output under recommended conditions consisting in a 50 mA sinewave. In that case -3 dB is obtained at 35 MHz. Figure 4.B illustrates the optical output under maximum allowed conditions consisting in a 100 mA sinewave. In that case, -3 dB is obtained at 30 MHz.

4.1.2. FLIM—The LED driver and laser diode have been compared by measuring the lifetime difference between ICG in DMSO and ICG in water. Data were collected as explained previously for each light source modulated at 30 MHz. Images were acquired every 10° for 3 consecutive phase periods with a camera exposure time of 100 ms and results fit to sinewave using Graphpad Prism. Fit results were scaled to the depth of modulation of the laser diode and plot for one phase period versus phase (Figure 5). Correlation between experimental results and the reconstructed sinewaves are between 98.0% and 99.7% with usually better correlation for the laser diode. On average, the phase difference measured is 7.07° with laser diode and 6.82° with the LED driver. This results in a lifetime difference of 0.658 ns using the laser diode and 0.634 ns using the LED driver.

4.2. Discussion

The theoretical dynamic limitation of the L760-AU LEDs, provided in their specifications for 50 mA driving current, is due to their rise and fall times of 160 ns total. The MOSFET rise and fall time, as provided in the specifications, is 26 ns total. This implies, if all these times are assumed to cumulate serially, a minimum period of 186 ns and a maximum full depth of modulation frequency around 5 MHz. Our circuit shows 85% depth of modulation at 5 MHz. In addition, the MOSFET input capacitance (35 pF) generates poles at 16 MHz and 32 MHz, as well as an increase in the circuit response within these ranges of frequencies (less than +3 dB in electrical response) as seen on the optical response (Figure 4).

The driver circuit is based on a potential difference on a resistor, and thus we need to keep this potential difference at the desired level. When using multiple drivers in parallel, current consumption is non-negligible. Ground variation, due to line resistance losses, can disturb the proper functioning of the circuit. To solve this issue, we chose to both minimize the line resistance and to reference all the grounds on the same common plane.

The purpose of the FLIM experiments was to prove the LED driver capabilities for lifetime measurements. While the recovered lifetime data was similar than with a laser diode (3.6% deviation on average), depth-of-modulation of the collected fluorescence under FLIM measurements was 60% lower with the LED driver (see Figure 5). This is mainly due to the fact that at this frequency the driver does not reach full depth of modulation on its optical output (in particular, it does not reach 0), contrary to the laser diode. Moreover, while not being critical, noise on the data was higher using the LED driver leading to lower correlation coefficient in reconstructing sinewaves.

It is also interesting to note that the photocathode of the IIT was modulated only by 100 Vpp due to hardware limitations. This modulation can be increased by 7-fold and would give higher depth of modulation on the acquired data.

5. CONCLUSION

We designed and constructed a low-cost, linear driver circuit capable of driving LEDs from DC to 35 MHz, at high power, and which permit fluorescence CW and lifetime measurements. The driver circuit has been tested in combination with a custom made LED board containing twelve 18 mW NIR LEDs. Both boards are assembled into modules and siliconized for heat dissipation. A single module can produce 100 mW of filtered light (35 nm FWHM). The modules show an optical -3 dB response at 35 MHz when used under recommended conditions and 30 MHz under absolute maximum conditions. FLIM capabilities have been assessed by combining the light module with an image intensifier, which permits heterodyne or homodyne phase measurements and we obtained similar results than using a NIR laser diode.

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Figure 1. LED DRIVER

Figure A. illustrates the principle of the LED driver circuit. Current is set through the voltage across sensing resistor isolated from the op amp by the transistor. Forward voltage is supplied independently and linearity is ensured by the feedback loop of the non-inverting circuit. Figure B. shows the implemented circuit. Additional resistors and capacitors have been placed to ensure stability.

Figure 2. FLIM setup

simplified schematic. An image intensifier (IIT) has been added to our fluorescence imaging system. The IIT gain is modulated at a frequency ω through its photocathode and the light source (LEDs or laser diode) modulated at the exact same frequency but with a controllable phase shift. FLIM experiment has been run at 30 MHz using a PC and images acquired using a custom-made Labview program. Images were then processed using GraphPad Prism.

Figure 3. DRIVER and LED BOARD

The LED driver board measures 25mm in diameter (Figure A. top view and Figure B. bottom view) and connects to a custom made LED board containing 12 LEDs. Finally both boards are molded together for heat dissipation.

Figure 4. OPTICAL RESULTS

from the LED driver and L760-AU LEDs from Epitex (Japan). Under recommended conditions with a 50mA current sinewave and -3 dB was obtained at 35 MHz (Figure A.) and at 30 MHz under maximum condition with a 100mA current sinewave.

FLIM results for LED and Laser diode

Figure 5. FLIM RESULTS

LED driver has been compared to a laser diode on a FLIM measurement. ICG in water and DMSO have been measured and lifetime difference differed on average by 3.6% between the two light sources. The experimental data have been fit to sinewaves with correlations greater than 98% for the LED driver and 99% for the laser diode. Results are plotted normalized to the depth-of-modulation of the fluorescence data from the laser diode.