BME Design-Spring 2020 - Ruochen Wang
Complete Notebook

PDF Version generated by

HANNA RAINIERO

on

Apr 29, 2020 @02:42 PM CDT

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Team contact Information

Jacky Tian - Oct 09, 2019, 2:28 PM CDT

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Project description

HANNA RAINIERO - Apr 29, 2020, 11:29 AM CDT

Course Number: BME 400

Project Name: Implantable Light Source

Short Name: Implant480

Project description/problem statement:

We are designing a device to more effectively photoconvert lung tissue in the mouse model kikGR33 for tuberculosis research and a separate device to photoactivate optogenetic rhodopsin channels in dendritic cells for dendritic cell activation.

About the client:

Our client Dr. Sandor is a researcher in the department of Pathology and Research Medicine at the University of Wisconsin-Madison.

Client Meeting 09/19/2019

HANNA RAINIERO - Sep 19, 2019, 6:35 PM CDT

Title: First Client Meeting

Date: 9/19/2019

Content by: Lisa and Hanna

Present: Lisa, Hanna, and Richard

Goals: To ask our client clarifying questions about the design goal and specifications regarding the project

Content:

- Looking at inflammation of the brain
- How cells are moving into the inflammation and or how cells are coming from the inflammatory area
- Genetic mice where you can see specific cell types and identifiable with colors
    - Localise where these cells are by changing their colors
- KikGER (green) mice
    - 2 types of mice
        - promoter
        - construct
- Cre kicks out genome and drives promoter to Kiker
    - Mouse is not green
- Cross mice with cre (2 types)
    - dendric cells green
    - myoric cells green
- Light mouse with 405 and 480 mice, it will emit red light
    - Laser was put into mouse head, turned portion of brain cells from green to red
    - **How immunity is ??? in the mice, understanding how cells come from the brain to inflammatory site**
    - **Immunity begins at lymph nodes, observed in mice**
- Tb contained by inflammatory lesions --> how fast do cells arrive there and are there any cells that escape from that are
    - Put laser near lungs
    - Do we see red cells elsewhere in green mouse
    - What is speed we see the cells green again (see speed of reaction)
- Problems with laser -- they are very small, TOO MUCH ENERGY AND HURTS CELLLS
- How big is the area that you light? --> **phototoxicity should not be excessive**
- The higher the penetration is better
    - Do research on light penetration
    - Optical nanobeads injected in surface and take light deeper (can go 5mm deep)
        - Helps to diffuse light and expand energy going into surrounding tissue
- Altered GFB mice, use light to pinpoint side
    - How are cells displaced
- The other project Prof Sandor is looking at is a cell expression of a light induced channel
    - Dendric cell to lymph node and activate to begin immunity
    - Whenever calcium get into cells, cells move to direction of lymph node
    - Make dendric cell function better or worse
- Other mouse, use light to detect site to understand movement
- In this mouse model, we want to see if a cell works or not (480nm)
    - Ontogenies used in neurons, light and neurons react and fire (or can create a construct to prevent firing)
    - Using this concept for immunization cells
    - Pulsing light at 15sec, after 15 min calcium gets into the dendrite --> light that emits for 1-2 hours on and off
        - This has been done in vitro
        - Device can be timed, record how many times it turns on and off
- There is competitor, he got cells that transfected with similar channels with similar characteristics, put back in mice (will be sent a paper for this particular author)
- 480nm light emitting diode turning off and on with the dendrites (brain)
- **Team needs to discuss if they need animal training for research purposes**
- Larger area, lower energy **ENDGAME --> understand cell traffic**
- Process to implant, put mouse to sleep, make trim, implant device for the duration of experiment, remove device, and sew the mouse up
    - 2 LEDs on the mouse at a time

        - Imaging is performed a few days/weeks later, remove tissue and organs, and observe percentage of red and/or green cell
        - What is speed of red cells replacing green
- Team should be familiar with mouse anatomy
- See also raw notes taken by Hanna below

Conclusions/action items:

HANNA RAINIERO - Sep 19, 2019, 6:35 PM CDT

Raw notes taken by Hanna:

Questions to ask Dr. Sandor:

- Where will the device be implanted? Chest? Head?
- Will the mice be sedated with the implant or will they be able to move around?
- At what wavelength will we be stimulating? 405 nm? 480 nm?
    - Size: about one square centimeter,
    - Expect on or on two sides
- What opsins specifically are we stimulating?
    - ChR2-tdTomato, ChR2-EYFP, eNpHR3.0, Ar
- ChR2(H134R)-tdTomato, ChR2(H134R)-EYFP, Arch-EGFP-ER2, or eNpHR3.0-EYFP
    -
- Budget? A few hundred? - nonexistent
- Other labs involved?
- We found that we could bulk order if that might be the case?
- What are you imaging on?
    - Fluorescent microscopes, **confocal microscope,**
- How many do you need of which wavelengths?
- Looking at immune trafficking- how cells change over time- fast replacement
- In tb you need some but not lot
- Granu inflammations, sarcoidosis, tb, we want cell turnover not collection, if cells don't move its difficult to treat,
- Drug that would help is already approved for something else and is just a different application drugs that impact vasculartization also have an affect on monocyte recruitment-
- Macular degeneration was helped by this devascularization drug
- Wavelength for specific locations?
- Can we test the lights in your lab?

Problem: working with immunology and infectious disease – mostly tb

Trying to understand how inflammation against bacteria works

Working with auto inflammatory disease as well – MS inflammation of brain

One thing we want to understand is how cells are moving into inflammation/ coming out of inflammatory side

Genetically created mice where you can see cell types and identify cells with colors

There are some fluids and molecules – they are using kikuma? Kk- green – whole mouse is green – recently they have one where bred with cre mouse- adds promoter to kk

Where is the cre that they are studying?

They are looking at mice with cre- 1 myeloid cells : macs, neutrophils as well as dendritic cells- immunity initiators

Optogenetics- if you light kk with 405 nm it will be red,

Recent MS paper uses kk mice w/ 405 nm light in brain- turned small portion of brain cells from green to red

Their question is how immunity is in use in the brain- they want to see where dendritic cells travel to and from the brain

Small hole in cranium- CSF lymph node near cranium

Kk mouse good for this model

Other place is in lung- inflammatory lesions- how fast do immune cells get to lesions. Rn putting laser next to lung and seeing if red lesion also time to returning to normal,

One problem is to use the laser- they have a small illuminated area- also too much energy

Will help to differentiate cell types

Some problems: how large is territory that you light, minimize phototoxicity, deeper into the tissue the better, they now have optical nanobeads which they inject which transmits light deeper changing light from 405 nm to 480 nm

Another type of mouse which are altered GFP mice but they use light to pinpoint a site where they can identify cell migration and accumulation at specific sites

Another project is a dendritic cell speficic expression of light indued channel protein- similar to tool box paper dendritic cell migration to lymph node

They want to look at 480 nm light calcium makes dendritic cells phagocytosis, the more they go the higher the immunity

What they want to do is control dendritic cell function-

In the one mouse light is used for detection

In the dendritic cell mouse- light is used for control of dendritic cells @ 480 nm

Optogenetics is often used in neurons- lighting causes neurons to fire or be silenced

Optogenetics helped a lot with neural networks

Now they would like to apply it to immune cells

They made the mouse and noticed w calcium sensors and putting light on/off 15 or 30 s

They need something to light 1-2 hours pulsating light

They did this in vitro

They now need something in vivo to time the light on and off

Another guy did something similar- instead of making mice that have this- he transfected cells and put them in the mouse- he will send us the paper

400 nm light and 480 nm light

480 they would like to be able to turn it off and on

Previous team gave them

Poster Presentation of Light Conversion 10/1/19

Lisa Xiong - Nov 16, 2019, 8:06 PM CST

Title: Poster Presentation of light conversion

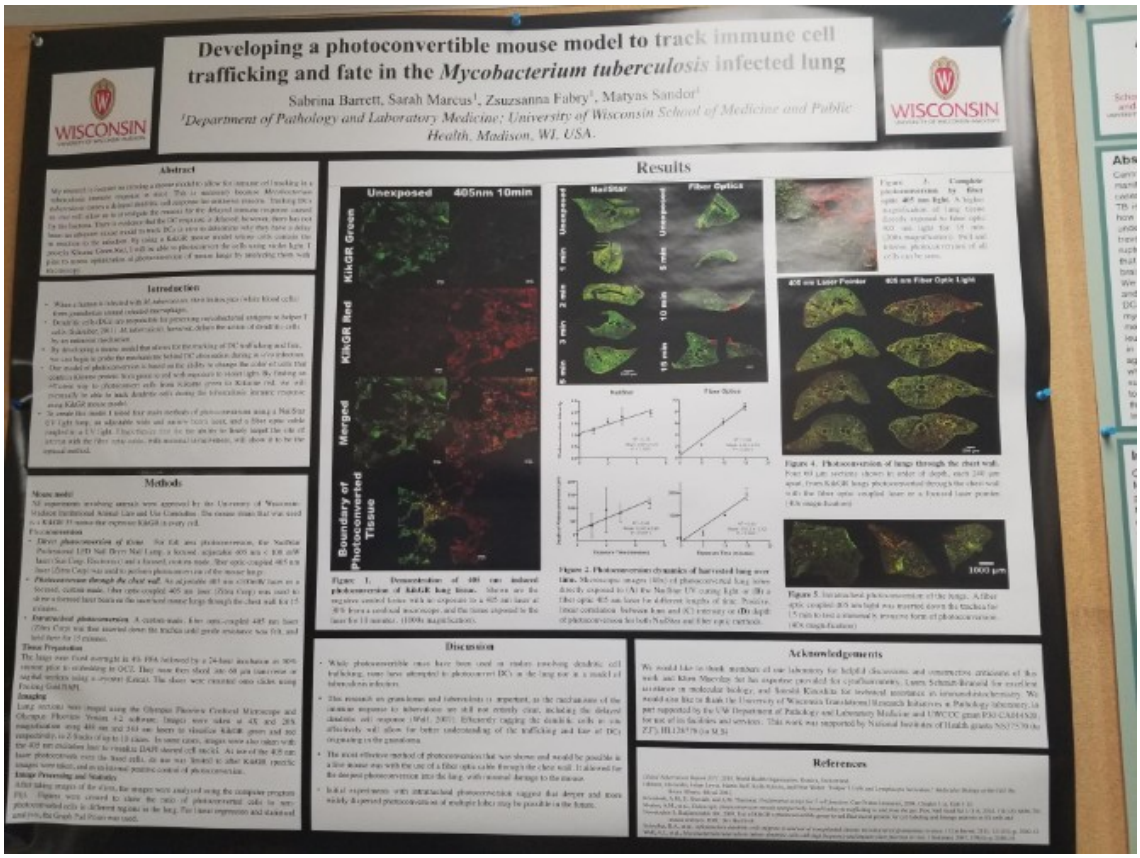
Date: 10/1/19

Content by: Team

Present: Team

Goals: To document the previous research poster presented in regards to our research

Content:

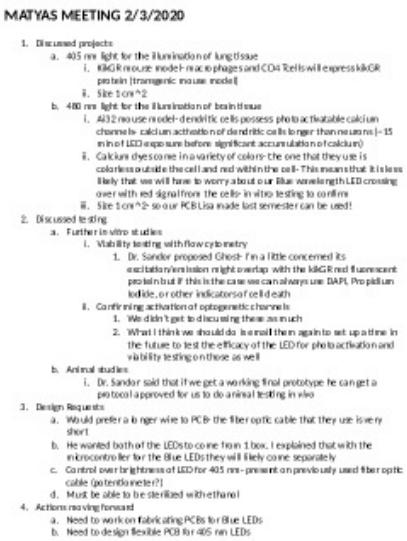


Conclusions/action items:

Photoconversion of the green cells will show us the travel of the red cells to replace the T-cells during their experiment.

Client Meeting 2/3/2020

HANNA RAINIERO - Feb 03, 2020, 5:05 PM CST



MATYAS MEETING 2/3/2020

1. Discussed projects
   a. 405 nm light for the illumination of lung tissue
      i. kiKGR mouse model- macrophages and CD4 T cells will express kiKGR protein (transgenic mouse model)
      ii. Size 1 cm^2
   b. 480 nm light for the illumination of brain tissue
      i. Ai32 mouse model- dendritic cells possess photoactivatable calcium channels- calcium activation of dendritic cells longer than neurons (~15 min of LED exposure before significant accumulation of calcium)
      ii. Calcium dyes come in a variety of colors- the one that they use is colorless outside the cell and red within the cell- This means that it is less likely that we will have to worry about our Blue wavelength LED crossing over with red signal from the cells- in vitro testing to confirm
      iii. Size 1 cm^2- so our PCB Lisa made last semester can be used!
2. Discussed testing
   a. Further in vitro studies
      i. Viability testing with flow cytometry
         1. Dr. Sandor proposed Ghost- I'm a little concerned its excitation/emission might overlap with the kiKGR red fluorescent protein but if this is the case we can always use DAPI, Propidium Iodide, or other indicators of cell death
      ii. Confirming activation of optogenetic channels
         1. We didn't get to discussing these as much
         2. What I think we should do is re-visit them again to set up a time in the future to test the efficacy of the LED for photoactivation and viability testing on those as well
   b. Animal studies
      i. Dr. Sandor said that if we get a working final prototype he can get a protocol approved for us to do animal testing in vivo
3. Design Requests
   a. Would prefer a longer wire to PCB- the fiber optic cable that they use is very short
   b. He wanted both of the LEDs to come from 1 box. I explained that with the microcontroller for the Blue LEDs they will likely come separately
   c. Control over brightness of LED for 405 nm- present on previously used fiber optic cable (potentiometer?)
   d. Must be able to be sterilized with ethanol
4. Actions moving forward
   a. Need to work on fabricating PCBs for Blue LEDs
   b. Need to design flexible PCB for 405 nm LEDs

MATYAS_MEETING_02032020.docx(14.7 KB) - download Notes from our meeting with Dr. Sandor

HANNA RAINIERO - Feb 03, 2020, 5:08 PM CST

Title: Client Meeting

Date: 2/3/2020

Content by: Hanna

Present: Hanna and Jacky

Goals: Clarify project goals and future testing and design

Content:

See attached.

Conclusions/action items:

1. Actions moving forward:
   a. Need to work on fabricating PCBs for Blue LEDs
   b. Need to design flexible PCB for 405 nm LEDs
   c. Boxing up both of them nicely, his old model had a power source that plugged into a wall outlet so it looks like that should be sufficient for ours
   d. It might be useful to confirm that the lab needs to modify the PWM for the Blue LEDs or if we can have a set PWM for them which would eliminate the need for interacting with the microcontroller and they could just turn it on and let it run
   e. Meet for testing with Martin and Dr. Sandor

Advisor Meeting 09/11/2019

HANNA RAINIERO - Sep 11, 2019, 1:00 PM CDT

Title: Advisor Meeting 09/11/2019

Date: 09/11/2019

Content by: Hanna

Present: All Team

Goals: Our initial meeting with our advisor to guide initial background research and brainstorm design and testing to further develop our prototype

Content:

Professor Williams specializes in MEMS and was very helpful in guiding our start to continue developing our LED's as an implant. See notes below from our meeting.

Notes:

-implant with external power source

-temperature of led might be a concern- heat sink- transfer heat from LED to metal- mass of metal should

TRPV1 channels may be triggered by too large of a temperature change in the mouse- 1 degree celcius

spread LED

Check out Justin's google scholar page for implantable light sources

Ed Boyden also does work with implantable light sources- decoupling light circuit from light emission? look at original paper

client is looking at implantable light at 405, 480 nm for 6 hrs

pulse with modulation turn on periodically- sync with ion channel firing? 50 Hz?

biomaterial- clear, insulated, dielectric constant: PDMS iffy dielectric constant, Parylene C more difficult to work with but there is a chamber in Justin's lab (currently down)

-mice are KIW-33

Next meeting- Sept 19th at 11AM

Conclusions/action items:

Between now and our next meeting we will continue background research and meet with our client before our PDS is due next week. Additionally, we will continue to brainstorm testing and implant design.

HANNA RAINIERO - Sep 11, 2019, 12:57 PM CDT

Advisor Meeting 09/25/2019

Jacky Tian - Oct 09, 2019, 2:28 PM CDT

Advisor Meeting 10/09/2019

Lisa Xiong - Oct 09, 2019, 2:06 PM CDT

Title: Post-Preliminary Presentation Advisor Meeting

Date: 10/9/2019

Content by: Lisa

Present: All

Goals: To discuss our preliminary presentation and get feedback on where we can improve

Content:

- Improve in areas addressed today
- Scores: 59 and 61 out of 82
- Improvements:
    - Background - Clarifying terminology and little more difficult for the average student
    - Restructure the presentation and have more upfront information
    - Competing Designs - Look at the optogenetic market
        - Clinical trial going on with implantable and use of optogenetic foot ulcer pain and retinol disease
        - Look at other research products
    - Quantification in PDS
    - Bring in a prop
    - Evolve the PDS - find a numerical way to tell client that it works
    - Put more weight on testing and statistics
    - Look at presentation evaluations/grading rubrics
- Poster
    - How did you test
    - Evaluation techniques
    - Comparison to PDS
    - Bringing it back to your goals
    - Prototype
- Parylene-C coating and issue
    - Justin's lab's coater is broken, has foreign contaminants
    - Single run is approximately $20
        - Requires student training + cost of materials
    - CLEAN room
        - Expensive because requires training
        - Premium usage fee
        - $80/hr includes training and making device (maybe up to $1,000)
    - Parylene-C can be available for **next semester**
- PDMS is a workable alternative for **this semester**
    - We care about water barrier and permeability
    - BME teaching lab
        - Contact BME 550 TA (good resource)
    - Buy a PDMS kit
    - Non-medical research, 100% silicone caulk from Home Depot
    - Polymerizes by cross-linking chemistry
- Maybe consider Norland Optical Adhesives
    - Often pops up in LED bond adhesives
- Yellowing of coating
    - Most of things we have talked about won't be affected unless in UV (but we are near)
- Testing protocol recommendations
    - Test temperature in the air
    - Water would conductively cool
    - Isolate the environment
    - See what has been published in the literature
    - IR thermometer in the design lab
- LED in series and parallel
    - 480nm LED has a driver
    - Circuit analysis would be nice to include in final report or poster presentation

Conclusions/action items:

The team could improve our project presentation by taking more time to go through the background and define some terminology. Justin had some feedback that some things discussed further in our presentation could be pushed forwards into our presentation. We should definitely discuss competing designs as well. The emphasis for the next evaluation will be testing and analysis, so the team needs to develop a good testing protocol. The team is on track otherwise for the project!

Team Meeting 09/16/2019

HANNA RAINIERO - Sep 16, 2019, 6:13 PM CDT

Title: Team Brainstorm Meeting

Date: 09/16/2019

Content by: Hanna

Present: All team

Goals: Brainstorm design

Content:

See attached image for PCB design sketches.

Notes:

- 1C threshold in mice
- Looking at heat sinks for LEDs-
- Dimensions of large LED 5x5 mm
- Dimensions of small LED 3.2 x 2.8 mm
- Pin length is 3.2
- Design matrix: Heat transfer, biomaterials, PWM
- PCB to connect similar points of LED- potentially flexible? Or in 2 parts?
- Questions for our Client:
    - Where will the device be implanted?
    - Will the mice be sedated with the implant or will they be able to move around?

Conclusions/action items:

Between Now and Thursday:

- Ruochen will make the PCB
- Asking Amit about Altium for PCB board
- Looking at patents of similar devices
- Check for thermal resistance calculations to predict heat sink size
- More background research
- PDS due Friday
- October 4th is presentations

HANNA RAINIERO - Sep 16, 2019, 6:14 PM CDT

IMG_7315.HEIC(657.5 KB) - download Image of Team meeting notes. PCB sketches, LED dimensions, LED/PCB/heat sink mapping.

Team Meeting 09/19/2019

Lisa Xiong - Sep 19, 2019, 11:31 AM CDT

Title: Team Meeting

Date: 09/19/2019

Content by: Lisa

Present: Lisa and Jacky

Goals: To discuss design points brought up last week and our current research so far.

Content:

- PCB board will be useful regardless
    - Reduce 16 wires to 5
        - Figure out do we actually need to power multiple LEDs (do we need all four?)
        - 4 wires would be enough to operate the LEDs
- LED has PWM built in to the device
- Optogenetics channel 50Hz
- Connector (biocompatible)
- PFC - Printed flexible connector (ZIF connectors) from Digikey
    - Connectors are 20 bucks a piece
    - Omnetics (Minneapolis) - expensive (LONG LEAD TIMES)
    - Imagineering for PCB boards
        - If you send them all your parts, they will assemble it for you
        - $1,500 to assemble, but they assemble a large amount for you
- Makerspace has PCB stations (where you can make your own)
    - They are a good to-go for help to diagnose simple design issues
- Reflow oven
    - Melts solder onto device --> if we pursue PFC we should consider this

Conclusions/action items:

Team Meeting 10/8/2019

HANNA RAINIERO - Oct 08, 2019, 6:18 PM CDT

Title: Team meeting to work on Preliminary report

Date: 10/08/2019

Content by: Hanna

Present: All team

Goals: finish the preliminary report and further develop our device

Content:

See Preliminary Report

Conclusions/action items:

We finished our preliminary report. We discussed attending the PCB manufacturing class held by the Makerspace next week on 10/15. We are meeting with Prof. Williams tomorrow to get feedback on our presentations and discuss our final design further with him.

Team Meeting 10/18/2019

HANNA RAINIERO - Oct 18, 2019, 6:24 PM CDT

Title: Team meeting 10/18/19 4:00PM to 6:30PM

Date: 10/18/19

Content by: Hanna

Present: All team

Goals: Finalize PCB Design and Testing brainstorm

Content:

Team Meeting

- Designed PCB Schematic on paper- lisa will do it on CircuitMaker and is meeting with Amit on Tuesday to confirm the design
- Idea for temperature sensing on board
- Went over arduino code
- going to talk with John G. Webster about in vitro testing
    - incorporating temperature sensing on PCB
    - Infared laser to detect temp of LEDs
- Future work: where we will order found a site with super fast delivery
- Challenges fabrication of PCB- solder pads?

Conclusions/action items:

Lisa will be making the PCB in Altium/CircuitMaker and is going to check with Amit next Tuesday to confirm our design. We then hope to test on a breadboard later that week. Hanna will be contacting John Webster to see about relevant *in vitro* testing.

Team PCB Class 10/15/2019

HANNA RAINIERO - Oct 19, 2019, 9:52 AM CDT

Title: PCB Fabrication and Manufacturing Class

Date: 10/15/19

Content by: Hanna

Present: All team

Goals: Gain a better understanding of PCB Design and Fabrication

Content:

Printed Circuit Board Workshop

A great first step is to make our prototype on a breadboard and test it to see if it works

Circuit Design

Softwares you can use:

- Altium designer: hard to use
- Autodesk Eagle: middle
- Fritzing: easiest

Step to make symbolic connections between multiple components circuit schematic

You can use trace width and length calculator – connections between componenets

Bantam mill and OMC mill – making the PCB yourself

Maybe we could make a connector on the pcb to output each of the wires to an Arduino

Export as a gerber

Upload gerber into your cnc mill program

Always do the outline last! Sections outlined in red let you know you need to switch tool tips

Makerspace is a good way to do proof of concept

PCBway is a pcb manufacturer that makes a labeled prettier board

Conclusions/action items:

The rest of this week we will be designing the PCB and hope to order it before November 9th.

Final PCB Design 12/9/2019

Lisa Xiong - Dec 10, 2019, 9:47 AM CST

Title: Final PCB Design

Date: 12/9/2019

Content by: Lisa

Present: n/a

Goals: To discuss the final PCB design, issues, and future work.

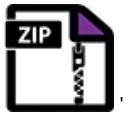
Content:

- Unlike designs 1 and 2, this PCB used polygon pours to create layers of power and ground that the power and ground pins of the LED connected to.
- The PCB designs 1 and 2 were non-functional because they utilized a thru-hole footprint and not a top layer footprint.
- This PCB board has three through holes
    - Vcc pin - This is the +5V used to power the LEDs
    - MCU - This pin connects the PCB to the microcontroller
    - GND - Connects the micrcontroller ground to the PCB

Conclusions/action items:

This is the final PCB that our team moved forward with. It succeeded the design checks and is supposedly functional. Unfortunately, the small size of the SMD footprints made it very difficult to solder the LEDs onto the board to check for functionality.

Lisa Xiong - Dec 09, 2019, 3:23 PM CST



PCB400FINAL.zip(33 MB) - download This is a zip file of the final PCB design our team came up with. The zip file contains the PCB project, schematic file, PCB file, PCB library and schematic library.

Team Meeting 10/18/2019

Lisa Xiong - Dec 10, 2019, 11:59 AM CST

Title: Team Meeting

Date: 10/18/2019

Content by: Lisa

Present: All

Goals: Discuss Circuit and LED connections

Content:

- The team met at the Makerspace to discuss Circuitmaker and Fritzer
- The team worked on wiring and importing parts for fabrication
- The team prototypes connections on paper.

Conclusions/action items:

The team made up a draft for the PCB connections.

Design Matrix for Biocompatible Coatings 10/9/2019

Lisa Xiong - Oct 09, 2019, 2:14 PM CDT

Title: Design Matrix for Biocompatible Coating

Date: 10/9/2019

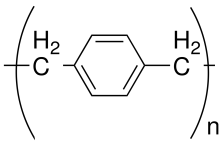
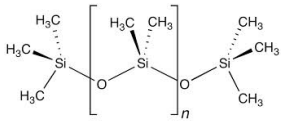
Content by: Lisa

Present: n/a

Goals: To document our design matrix and our process of choosing Parylene-C as our final contender.

Content:

Table 1: *Design Matrix for Biocompatible Coating*

Criteria (weight)	Parylene	PDMS	Mastersil 151 Med
			
Biocompatibility (40)	5/5	3/5	4/5
Ease of Fabrication (25)	3/5	4/5	5/5
Permeability (13)	5/5	2/5	4/5
Optical Clarity (10)	5/5	4/5	4/5
Flexibility (7)	3/5	4/5	5/5
Cost (5)	5/5	5/5	4/5
Total (100)	87.2	67.8	86.4

Safety (Biocompatibility)

Safety is defined as the “biocompatible rating” of the material. Since the light emitting diodes will be implanted into the mouse for a maximum of two hours, the biocompatible .materials must be able to protect the electronic components and repel the organic fluids. The material also must not trigger inflammation or an immune reaction within the mouse.

Safety was ranked as the second most important criteria with a weighting of 20%, because we need to keep the mouse alive and with little inflammation to ensure the data our client collects is reliable. We decided that the material with the most biocompatibility was parylene because it is FDA approved for implantation in the body and has low permeability to water and is both chemically and biologically inert. While medical grade silicone and PDMS have similarities with parylene, they lack the extremely low permeability to water that parylene offers which ensures are device will not harm the mice and the electronics will be safely isolated from the bodily fluids. Parylene C is considered the gold standard for devices implanted that need to resist both moisture and chemicals.

Permeability

Permeability is the extent to which the material resists absorbing water and/or chemicals. For our implant we need an effective barrier that will not allow chemicals or water to damage the electronic circuits. Due to its implications with integrity and longevity of the device, we rated Permeability at 15%--tied for the third most important criteria for our device. Parylene had the highest score due to its very low permeability to water and chemicals while medical grade silicone and PDMS are susceptible to chemicals and water permeating through the material. This would put the electronics within the implant at risk of damage.

Cost

Our cost is ranked as the lowest criteria, weighting 5%, because we have some freedom to use our budget provided by our client and also because most of the synthesis of biomaterial is possible to be manufactured in labs here at UW-Madison, potentially at low costs. Therefore, our team considers cost to be a less critical factor in our design evaluation.

Optical Properties

Parylene-C is vapor deposited and the most optically clear. It is very beneficial thanks to its very thin coating. Also has very low water permeability.

Ease of fabrication

Ease of fabrication is an important factor in our design evaluation and our team gives a weighting of 25%. To choose the proper biocompatible material for coating our designed device, our team needs to consider whether our team is able to manufacture the material, or through online purchase, in this semester with the sources our team can acquire. Our team has experience in fabricating and using PDMS so our team agrees that PDMS can be easy to fabricate within this semester. Also, we have found some labs on campus that can manufacture PDMS. For the medical grade silicone, our team did research on different forms of silicone in manufacturing and found that the liquid injection might be a promising and manageable method for our project. Therefore, our team gives 4 out of 5 to PDMS and medical grade silicone in terms of ease of fabrication. For the parylene, our team should do more research on the fabrication method of parylene , which is beyond our scope, and whether parylene can be manufactured following procedures our team can actively participate in. Therefore, for the unknown characteristics of this material, our team gives 3/5 to parylene.

Flexibility

Since our device will be implanted into the mice and our client wants our device to be adjustable to deliver light to different regions instead of focusing light on a specific area for a period of time, the biomaterial our team chooses should also have the flexibility to meet this criteria. Overall, our team agrees that medical grade silicone has the greatest flexibility of the three based on advice from our advisor and Dr. Amit Nimunkar so our team gives a 5 out 5 to the medical grade silicone. For PDMS and parylene, our testing results from previous semester's work shows that there is some flexibility but the flexibility of those two materials may not be as easy to manipulate as the medical grade silicone. Therefore, our team assigns lower score for PDMS and parylene.

Design Descriptions

1. Parylene

The unique parylene polymer series was isolated in the 1940s. Parylene has become the protective coating of choice for challenging electronics, aerospace and medical applications and has a Young's Modulus of 3.1 - 4.75 GPa. Parylene is characterized as chemical and biological inert, low water permeability and absorption, which are the preferred characteristics to our project. There are existing designs from research groups that utilizes Parylene C as encapsulation materials and substrate for intraocular pressure (IOP) monitor [4] and neural electrodes for recording [5].

2. PDMS

PDMS is short for polydimethylsiloxane. It is a material that has a Young's Modulus of 360-868 kPa. The low Young's Modulus also contributes to its unique flexibility. It has strong dielectric strength, biocompatibility and low chemical reactivity. These properties made it a candidate for our encapsulating material of the device. Since it is flexible and high dielectric strength, it could be used for pressure sensing by changing its capacitance because of the pressure. Some other groups have also used the PDMS as the materials for IOP monitor [2]. It is light transparent in the visible region and highly absorbent at some wavelengths in the near infrared region.

3. Medical grade silicone

Medical grade silicone is FDA approved to be used in biomedical implants. It is biocompatible and is quite flexible over a wide range of temperatures. It has a Young's Modulus of 360-868 kPa, resulting in high tear strength and high tensile strength and it is more flexible compared with PDMS.

The strong Si–O–Si (siloxane) backbone offers strong chemical inertness as well as its flexibility, medical grade silicone could be used as biomaterial with strong biocompatibility for implantable medical devices.

Since it is also transparent and has high refractive index, with its flexibility and biocompatibility, a group made contact lens for IOP monitoring with resonance circuit embedded in the material [3]. Furthermore, other group has used it to encapsulate the printed circuit board (PCB) with this material for intracranial pressure (ICP) [1].

Conclusions/action items:

The team will move forward with Parylene-C as our biocompatible coating.

Design Matrix for Circuit Designs 12/10/2019

Lisa Xiong - Dec 10, 2019, 11:55 AM CST

Title: Design Matrix for Circuit Designs

Date: 12/10/2019

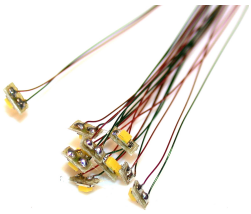
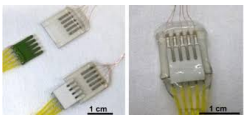
Content by: Lisa

Present: n/a

Goals: To show our design matrix for how we wanted to power the LEDs.

Content:

Design Matrix for Electronic Circuit Design

Criteria (weight)	Pin and wire 	PCB integration 	Implantable connectors 
Safety (30)	3/5	4/5	5/5
Ease of Use (30)	2/5	4/5	2/5
Stability (20)	2/5	5/5	4/5
Ease of Fabrication (15)	2/5	4/5	3/5
Cost(5)	5/5	4/5	3/5
Total (100)	49	84	70

Safety:

Safety was ranked as the most important criteria with a weight of 30% because we need to protect the mouse from the electricity we are powering our LEDs with and prevent the mouse blood from seeping into the electronics. The electronic circuit design should prevent electrocution. The pin and wire design was ranked the lowest because of the 16 wires that would be needed to operate the LED. These 16 wires would have current running through them which could potentially be fatal to the mouse. To improve its safety would require coating the wires or covering them with protective plastic which would increase the time needed to fabricate the LEDs. The PCB board was ranked next highest because it would consolidate and simplify the wires connected to the LEDs. The LEDs would be powered via the PCB board, but would still require power wires to be insulated. The implantable connector was rated highest because they are designed to be operable in wet environments. Implantable connectors utilise a biocompatible and secured container which houses the electronics. There is a biocompatible and flexible substrate which provide the users with access to the device.

Ease of Use:

Ease of use was ranked second with a weight of 30% because we needed to make sure our design would be simple and easy to use for our clients. Our clients do not have an electronic background, and ideally they could activate the LED and associated program using a microcontroller. The pin and wire was ranked one of the lowest because we were concerned the wires would confuse the connections to and from the microcontroller. The implantable connectors were also ranked low, since more complex designs would need to be involved to allow the LEDs to become functional. The PCB board was ranked highest because we could power multiple LEDs with the PCB board, consolidate the number of wires, and decrease confusion to our client.

Stability:

Stability was ranked third with a weight of 20% because we needed to consider how much movement would be involved once it is in the mouse. The pin and wires were ranked lowest because the sixteen wires would cause more movement in the mouse. The implantable connectors were ranked second highest because they would apply differently in the head compared to the chest cavity. The PCB board was the most stable because it would have the LEDs wired on a single entity, which reduces the movement inside of the mouse.

Ease of Fabrication:

Ease of fabrication is the second least to consider since we have many electric circuit fabrication method and biomaterial fabrication available both on campus and online. Therefore the ease of fabrication is less of consideration for the design matrix. The PCB board scored the highest in this criteria because it could be designed online and then either made at the Makerspace or sent to a company to create for us. The benefit of the PCB board is that it can be reproduced for future uses in case our client needs more LEDs.

Cost:

Cost was ranked the least with a weight of 5% because the criteria for device's performance is more important than the cost. Moreover, for our current design, the most expensive material is the biomaterial that coats it. Our client also had little or no limitation on the materials that we need to purchase less than 1000 dollars, and the materials used in the design is well below it. So it is the least important factor to our current project.

Design Descriptions:

1. Pin and Wire

The pin and wire design is designed by the last group. The design have each tiny LED (5mm*5mm) soldered with the thin wires to each pin respectively. The design then integrate 4 such LEDs on top of an insulating board, and let their wires go through the holes in the board. The LEDs are fixated on the board with glues and the biomaterial chosen will then coat the complex to make the design complete.

The design utilized common materials: thin wires, and insulating board with holes to address the problem. However, there are some disadvantages and the problem with fabrication process discovered in the process of fabricating it.

The soldering is not as stable as the last group thought and could easily come off during further fabrication process, such as integrating the LED on the board. Therefore we scored 2 and 3 for its safety and stability criteria. If the pins-wires connection was broken during the process then it is neither reliable nor safe for mice.

In the last design, we chose LED with adjustable wavelength for achieving the target wavelength (480 nm), so that there were 4 pins for each LED that needs to be soldered. For each device, there were 4 LEDs on the board and that sums up to 16 wires that needs to be connected for powering the device for normal function. The messy wires, though the wires connecting to the pin with the same function on each LED were taped together for discrimination, would be trouble for both our client and group for fabricating. Therefore we rated the ease of use as 2 out of 5. If the client had no experience in electric circuits, the device could be connected to the wrong pins and the device would not function as desired.

The fabrication process is not optimized and streamlined for each device, the small pins are hard to solder to wires and glue the LEDs on the board is difficult as well. So we gave the ease of fabrication criteria as 2 for the design.

2. PCB Integration

This design is an extension of the concept of placing the LEDs on a board as the last design. However, this design integrates the LEDs directly on the printed circuit board (PCB) with soldering, so that there is no glue needed for fixating the LEDs on the board. By printing circuit on the board, we also eliminate further wire usage since we connect the pins with circuit board. Therefore less wires are required for connecting the board. So we rated 4 on "Safety" and stability criteria, since we have less chance of having pins to fall off and connections to be broken with less wires. We also rated 4 out of 5 for ease of use because client would only need to connect one wire for each function instead of 4 wires in the last design. It is easier to fabricate because we could use overflow oven available on campus for soldering. It would cost similar to the last design with more budget spent on ordering of the materials.

3. Implantable Connectors

The implantable connectors are an improved modification of the pin and wires. Instead of having 16 wires extending from the LEDs, the wires would be consolidated through a customizable, flexible, compatible, and implantable substrate. The implantable connector would be attached to a secure compartment which would contain the electronics to power the LEDs. Although these connectors are suited for the environment our LED will be operating in, it scored second highest because of the cost and ease of fabrication. The team would need to spend money to purchase the correct materials for the implantable connectors, and the fabrication would be difficult since the resources to create the connections on the flexible may require high technology machines. It would be challenging to design connections on a thin substrate layer.

Conclusions/action items:

Our team moved forward with the PCB integration design.

Team meeting 2/28/20

HANNA RAINIERO - Apr 29, 2020, 11:36 AM CDT

Title: Team Meeting 2/28/20

Date: 2/49/20

Content by: Hanna

Present: all team

Goals: plan out project further

Content:

See attached notes.

Conclusions/action items:

See attached notes.

HANNA RAINIERO - Apr 29, 2020, 11:36 AM CDT


Project future work:

Friday 2/28/20

Meeting with Justin- All

Printing PCB- All

Call Plastics 1 - Hanna

Start Solidworks for Box- Hanna

Look up PDMS protocol- Jacky

Printing PCB – Lisa

Fabrication of PCB – Ruochen and Lisa

PDMS coating of PCB- Hanna and Jacky

Meeting with Sandor – All

Contact Anit about Spectrophotometer – Lisa

Project_future_work.docx(12.1 KB) - download

Material Costs 12/9/2019

Lisa Xiong - Dec 09, 2019, 3:31 PM CST

Title: Material Costs for Fall of 2019

Date: 12-9-2019

Content by: Team

Present: All

Goals: To document the cost of our prototype for the Fall semester of 2019.

Content:

Material	Quantity		Cost
Printed Circuit Board (PCB)	10		$43.00
DotStar 5050 RGB LED	20		$47.10
5050 LED Breakout PCB	10		$15.97
Microcontroller and Circuitries	N/A		$0.00
Ocean Optics Spectrometer	1		$0.00
		Total	$106.07

The majority of our costs actually came from shipping fees.

Conclusions/action items:

For this semester, our team spent $106.47 on our prototype that is functional for photoconverting KikGR33 mouse cells!

Breakout Boards with 480 and 405 nm LEDs 12/10/2019

Lisa Xiong - Dec 10, 2019, 11:11 AM CST

Title: Breakout Boards with 480 and 405 nm LEDs

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document how we soldered the LEDs onto the breakout board and show what the final prototype looked like.

Content:

- The 480 nm LED is a type of 5050 led. It is compatible with a breakout board that is available on Adafruit that already has SMD pads for this size and type of 5050 led.
    - The PCB has 6 pads but we only used the outer four
    - Header pins were soldered at the through holes to connect to a breadboard
- The 405 nm LED is much smaller and thankfully only two pin
    - Two 405 nm LEDs could fit on the break out board, so we connected two in parallel to the header pins

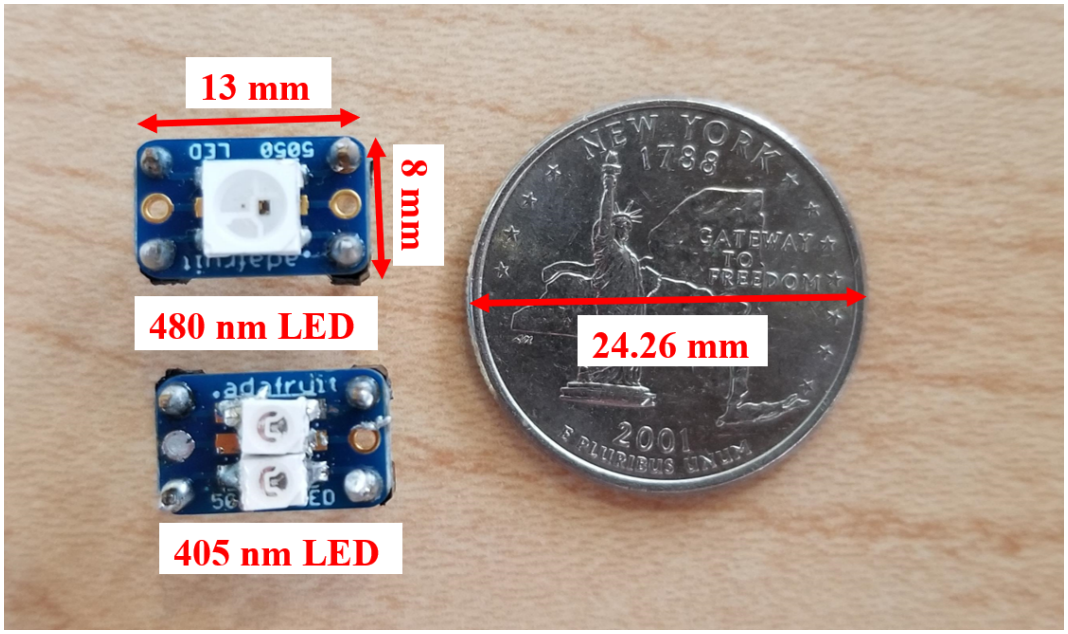


Figure 1: *The breakout boards with the LEDs are compared to the size of a quarter. This is the final prototype that we tested with.*

Conclusions/action items:

The team successfully developed a working prototype for debugging and testing connections to and from the microcontroller to other LEDs.

Final PCB with 480 nm LED 12/10/2019

Lisa Xiong - Dec 10, 2019, 11:15 AM CST

Title: Final PCB with 480 nm LED

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document our final PCB prototype.

Content:

- The 480 nm LED fit well onto the PCB
- SMD footprints are very close together, their small size made it very difficult to apply solder paste
- The through holes were a little small (tolerance was too small), so future work would be to make it larger to fit a 22 gauge wire and make the SMD footprints larger

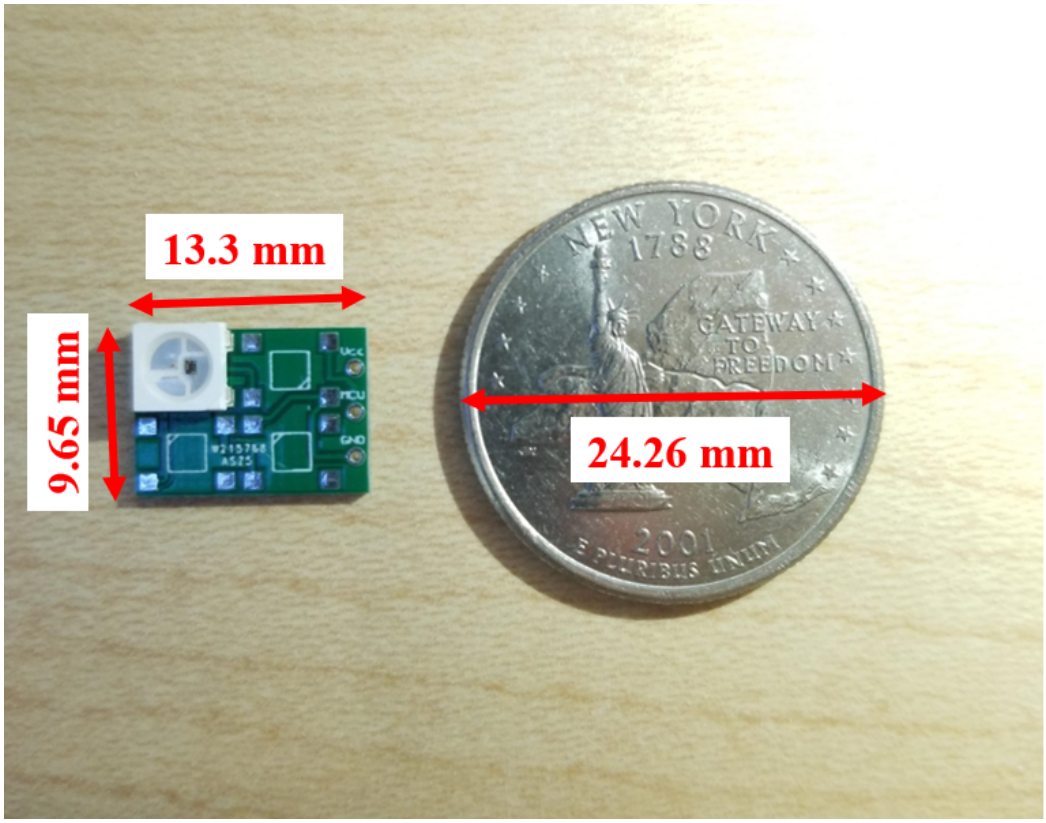


Figure 1: Comparison of the final PCB to the size of a quarter. A 480 nm LED is placed on the PCB to show the relative size between the PCB board and LED.

Conclusions/action items:

Although the team could not check for the functionality of the PCB due to soldering difficulties, it was great to know we could design our own customized device for powering and controlling the LEDs.

Lisa Xiong - Dec 10, 2019, 4:32 PM CST

PCB400FINAL.zip(33 MB) - download This is a zip file of the final PCB design our team came up with. The zip file contains the PCB project, schematic file, PCB file, PCB library and schematic library.

Bantam Printed PCBs 4/29/2020

Lisa Xiong - Apr 29, 2020, 2:06 PM CDT

Title: Bantam Printed PCBs

Date: 4/29/2020

Content by: Lisa

Present: n/a

Goals: To document the printed PCBs that were prepared before spring break.

Content:

Unfortunately, I cannot access the Altium PCB files and the Bantam files that I used to print the PCBs at the MakerSpace because they are on my CAE account. I have used CITRIX in an attempt to access and download the files, but they are not visible on the remote server. What is shown here are images and the fabrication process of the PCBs produced this semester. Due to COVID-19 outbreak at the beginning of 2020, our team felt that timely delivery and manufacturing of PCBs from PCB manufacturers would be affected. As a result, we chose to print at the MakerSpace to allow for testing of PCB schematics and connection debugging. When students are allowed to return campus, I can attach the appropriate documents to this page. For now, I will attach schematics and images of the final PCB.

- **405nm -** A, The 405 nm LED is a 2 pin device, powered with 0-3.3 V (pin 1) and connected to ground (pin 2, units in mm) [18]. B, LTSpice was used to create the circuit schematic. The PWR symbol represents a power supply of +3.3 V which is input into pin 1 of the LED represented by the triangle-vertical line symbol. It is then connected to the ground.

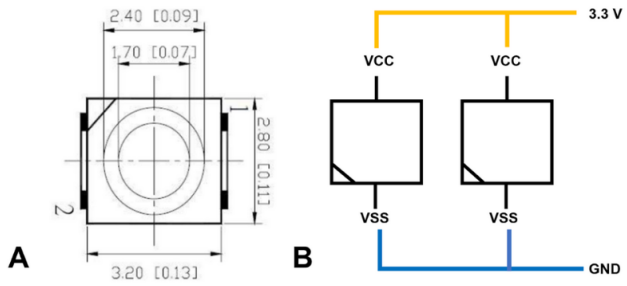


Figure 1. *Image of the 405nm connections and schematic.*

- **465nm** - A, The 465 nm LED is a 4 pin device. Pin 1 (VSS) is the ground pin, pin 2 (DIN) is the digital input pin that communicates with the microcontroller, pin 3 (VDD) is the power pin where +3.3 V is input, and pin 4 (DOUT) is the digital output pin where the LED can send the signal it receives from the microcontroller to other LEDs [19]. B, The 465 nm LEDs were powered in parallel (+3.3 V) through the Vcc pin of the microcontroller (represented by the Input2 symbol), connected to ground through the GND pin of the microcontroller, and the LED designator 1 communicated to the microcontroller (pin 2 LED to pin 1 of Input2).

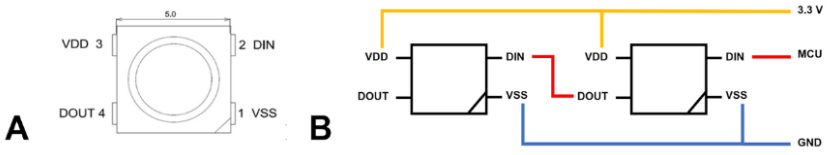


Figure 2. *Image of 465nm connections and schematic.*

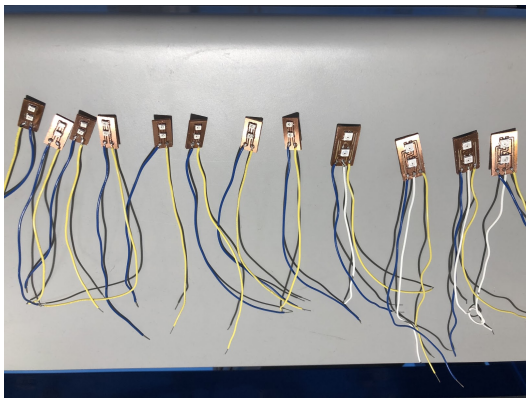


Figure 3. *405 nm and 465 nm final PCB prototypes printed by the Bantam mill.*

Conclusions/action items:

We successfully printed the PCBs for prototyping and in-vitro testing.

ledMOUSE Testing Protocol 12/10/2019

Lisa Xiong - Dec 10, 2019, 11:38 AM CST

Title: ledMOUSE Testing Protocol

Date: 12/10/2019

Content by: Hanna

Present: n/a

Goals: To document the testing protocol we did to measure the LED intensity and wavelength using OceanOpctics Spectrophotometer (USB2000+).

Content:

LED Brightness and Intensity Testing

1. Place the LEDs in a dark space under the ocean optics spectrophotometer 12mm from light receptor. See image.

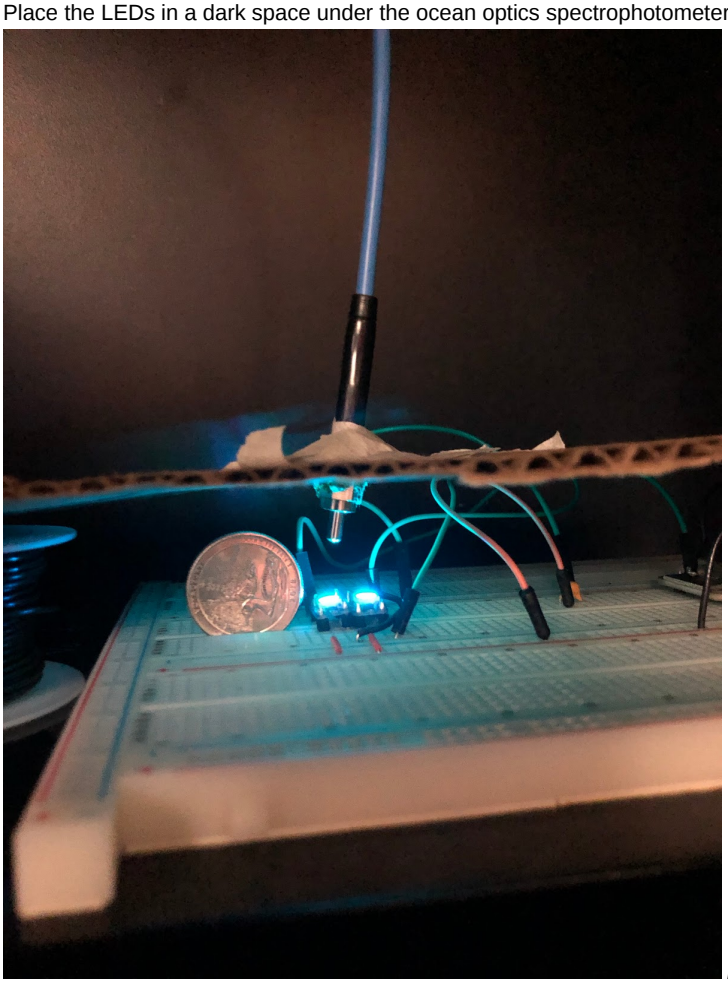


Figure 1: *Image of testing setup*

2. Type in commands in the Arduino Serial Monitor to light up the LEDs. An example could be for 480 nm LEDs from pin 2 at 4% brightness for 10 seconds with half second pulse width modulation is:
    1. [2/c?480]
    2. [2/b?10]
    3. [2/f?1000:0.5:10]
        1. The format for entering the color, brightness, and illumination frequency is
            1. [<pin number>/c?<wavelength>]
            2. [<pin number>/b?<brightness>]

3. [<pin number>/f?<period (ms)>:<duty cycle (decimal):total duration (s)>]

3. Capture the spectra on Ocean Optics and convert to a txt. File for MATLAB analysis
4. Analyze the file in MATLAB.
    1. See code:

```
file = &#39;...';

A = load(file);

reference = [470.2540, ...

470.6100];

wavelength = A(400:1400,1);

intensity = A(400:1400,2);

Light_Energy = zeros(size(wavelength,1),1);

for i = 1:size(wavelength,1)

Light_Energy(i,:) = intensity(i,:) * 10 * 3e8 *6.63e-34*1e9/(wavelength(i,:));

end

p = plot(wavelength,1000*Light_Energy*10000/(0.025^2*2048*14e-6*200e-6),&#39;b-

&#39;,&#39;LineWidth&#39;,2);

ylabel(&#39;Light Intensity (mW/cm^2)&#39;);

24

xlabel(&#39;wavelength(nm)&#39;);
```

In vitro photoconversion testing:

Photoconversion consisted of 5-min exposures, once per day at 15 d.p.i and 16 d.p.i. of EAE. Mice were harvested at 17 d.p.i. to allow visualization of photoconverted cells after 24 and 48 h (Supplementary Fig. 1). The heads were fixed in 4% PFA overnight, which although lowers the photoconverted signal intensity of the Kikume protein, is still obvious by microscopy77,78. Additionally, fixation is required prior to decalcification. This protocol causes a localized photoconversion within the CNS parenchyma, yielding approximately 7% photoconversion of cells by area per brain section.

Conclusions/action items:

This is the testing protocol our team used to measure the intensity and brightness. The cardboard helped to stable the cable and keep the receiving end of the cable at a constant distance.

Temperature Testing Protocol 12/10/2019

Lisa Xiong - Dec 10, 2019, 8:46 PM CST

Title: Temperature Testing Protocol

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document how we measured the temperature of the LEDs.

Content:

1. LEDs and header pins were soldered onto the breakout board
2. The breakout board were connected to the microcontroller/power source and ground
3. The LEDs were then turned so that the back of the LED and the break out board PCB was sticking out at us
4. For 5 minutes, in 30 second intervals, temperature was measured from the back of the LEDs using an infrared laser heat gun (Fig. 1).

Figure 1: *Image of the testing procedure. The LED was connected to a breadboard and suspended with the breakout board facing us. An infrared laser heat gun was used to measure the temperature.*

Conclusions/action items:

Using this protocol we measured temperature from the back of the LEDs to see if it would rise to temperatures of 50 to 60 degrees Celsius.

In Vitro Testing protocol 12/10/2019

HANNA RAINIERO - Dec 10, 2019, 9:07 PM CST

Title: In vitro testing protocol with KikGR cells

Date: 12/10/2019

Content by: Hanna

Present: All

Goals: To create a standard protocol for in vitro testing that we may reference in future studies

Content:

In vitro LED exposure of cell suspension of KikGR lymph node cells (see photo)

1. Pellet the cell suspension in an 1.7 mL clear conical tube.

2. Place tube directly on top of LED for 5 min and 15 minutes

3. After exposure time resuspend cells in PBS and pipet onto a slide counter for ease of imaging

4. Image on a confocal microscope with **no** exposure to 405 nm wavelength light, the Kikume protein emits 517 wavelength light (green) under a fluorescent microscope when excited by a green laser (488 nm). **With** exposure of a 405 nm wavelength, the Kikume protein should undergo a conformational change and emit red (593 nm) when visualized under a fluorescent microscope after excitation with a red laser (594 nm).

5. After imaging make a 1:1 uL amount of Trypan Blue:Cell Suspension and assess cell viability.

Conclusions/action items:

With this protocol we may standardize future in vitro testing as we look at the efficacy of our device to photoconvert and photoactivate tissue.

Temperature in vivo and in vitro Testing Protocol - 2/26/2020

Lisa Xiong - Feb 26, 2020, 10:34 AM CST

Title: Temperature *in vivo* and *in vitro* Testing Protocol

Date: 2/26/2020

Content by: Lisa

Present: n/a

Goals: To document the testing protocol for measuring the change in temperature of a phosphate buffer solution (PBS) from a PDMS encapsulated PCB.

Content:

1. Why do we need this test?
    - This test is required so we can make sure that the temperature coming from the LEDs and PCB does not change the 'systemic body temperature' of the mouse by more than 1 degrees Celsius. If the PBS's temperature exceeds 27 degrees Celsius, that means that it may not be suitable for use in the mouse body.
2. Testing protocol
    - Change in temperature of the LED in vitro/in vivo was simulated by measuring the change in temperature of phosphate-buffered saline (PBS) solution with the PDMS encapsulated PCB over a duration of two hours (Fig. 1).
    - The temperature of the PBS should be measured every 10 minutes for the duration of 2 hours. The duration of the test is 2 hours since that is the average length of the study at the Sandor Lab.
    - After the test, the data should be analyzed either in excel or any other statistical software that can perform a regression analysis to look at the temperature variation and to see if it stayed below the temperature threshold.

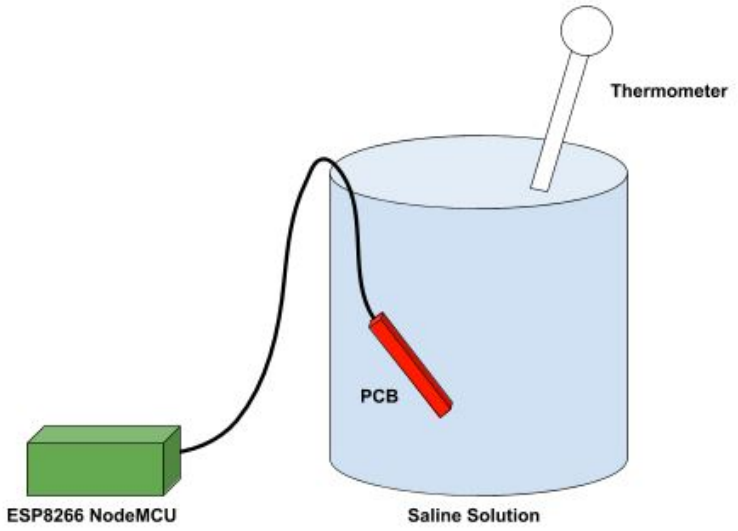


*Figure 1**.** The PDMS encapsulated PCB is placed in a saline solution and connected to the microcontroller. The starting temperature is 20°C (room temperature) and recorded every 10 minutes for two hours.*

Conclusions/action items:

This is the test that will be performed so that you can measure the change in temperature from the PCB and LEDs.

405 and 480 nm Testing Protocol 4/27/2020

Lisa Xiong - Apr 27, 2020, 9:53 PM CDT

Title: 405 and 480 nm Testing Protocol

Date: 4/27/2020

Content by: Lisa

Present: n/a

Goals: To document the testing protocol for the PDMS and non-coated LED at home. This testing procedure is much different since it was less formalized as a result of COVID-19.

Content:

The team was interested in four variables when comparing PDMS encapsulated LEDs to non-encapsulated LEDs: wavelength, intensity, voltage, and 'program' brightness.

1. Wavelength vs. Intensity (for both 405 and 480 nm LEDs)
    - The team hypothesized that there would be a significant influence of PDMS encapsulation on LED wavelength and intensity measurements.
2. Voltage vs. Intensity (ONLY for 405 nm LEDs)
    - The 405 nm LEDs are not programmable like the 480 nm LEDs. To control the brightness and intensity of the 405 nm LEDs, you have to control the voltage/current that is supplied to the LED. The team was interested in understanding the voltage vs. intensity behavior of the 405 nm LED.
3. Brightness vs. Intensity (ONLY for 480 nm LEDs)
    - The 480 nm LEDs are programmable to control the wavelength, brightness, and pulse width modulation. The team was interested in understanding the brightness vs. intensity behavior of the 480 nm LEDs.

The following are the testing procedures for each test:

1. For wavelength and temperature testing, an Ocean Optics Spectrophotometer (USB2000+) was used to collect wavelength and intensity data from the LEDs (Supplement X). In order to minimize saturation of the spectrophotometer, the LEDs were kept at a distance of 35.81mm from the spectrophotometer (Fig. 1). A similar testing setup was done for the 405nm LEDs. However, because of the non-programmable LED intensity, the sensor was placed at a much further distance of 659.16mm. Ten wavelength and intensity data was collected to identify the consistency of the LEDs with standard error calculations and to identify the mean wavelength range and mean peak within the required intensity range for each of the LEDs. Measurements of PDMS coated and uncoated LEDs were also measured to compare the effect of PDMS on the LED wavelength and light intensity.

2. When the 405nm LEDs are connected to a 3.3V power source, the LEDs will emit the maximum light intensity at a 405nm wavelength. To develop a user-friendly method of controlling light intensity, a three pin linear rotary potentiometer was connected between power and the LED to limit the input voltage. The potentiometer allowed for control of resistance and voltage supplied to the LED using a dial. The 405nm LEDs were set at a perpendicular distance of 659.16mm from the spectrophotometer sensor. A digital multimeter was used to measure the voltage between VSS and Vout at the maximum light emittance to the lowest visible light emittance. Intensity of the 405nm LEDs were measured at the following voltages: 2.84V, 2.88V, 2.93V, 2.97V, 3.03V, 3.06V, 3.08V, 3.10V, and 3.15V, where 3.15V was the maximum voltage measured when the dial was at its minimum resistance. Three measurements were taken at each voltage step. Intensity of the PDMS coated and non-coated LEDs against voltage were measured and analyzed with linear regression.

3. The programmed brightness of the 465nm LEDs can be used to control the intensity of the LED light. The testing setup of the 465nm LEDs is the same setup mentioned in section 2.4.1. Three intensity measurements were taken at five levels of arduino code brightness: 1, 2, 3, 4, and 5. Their corresponding real-time brightnesses are 0.39%, 0.78%, 1.18%, 1.57%, and 1.96%. Intensity of the PDMS coated and non-coated LEDs against program brightness were measured and analyzed with linear regression.

Conclusions/action items:

These protocols are what we used to analyze the four variables that we were interested in: wavelength, intensity, voltage, and 'program' brightness.

Gelatin Phantom Testing protocol

HANNA RAINIERO - Apr 29, 2020, 11:33 AM CDT

Title: Brain gelatin phantom test setup/protocol

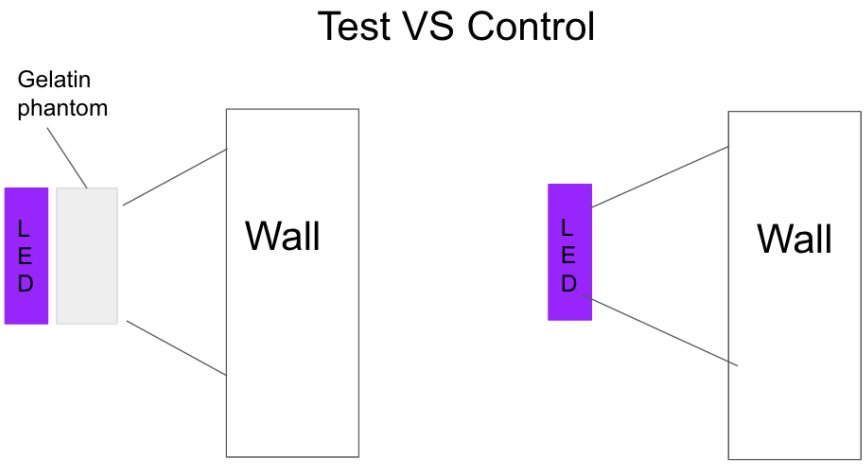
Date: 4/29/20

Content by: Hanna

Present: n/a

Goals: Identify light scatter properties while we are unable to access in vivo studies in lab

Content:



Experimental Setup.

The light scattering pattern in the brain was simulated by shining the 405nm LED through the brain tissue phantom made with gelatin to the wall in a dark room. The same 405nm LED is shined with the same distance away from the wall as the control to compare the difference. The brain tissue phantom gelatin is made with 50% of the water replaced by milk, and it exhibits similar photoacoustic properties to that of the brain tissue. The light scattering pattern on the wall was recorded by taking a photo with an iphone and the image is further processed with imageJ to measure the scattering of the light.

link to paper reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4490606/

Conclusions/action items:

We hope to use phantoms to simulate *in vivo* light scatter properties while we are unable to go into Dr. Sandor's lab. For future testing we may want to quantify further the results with a spectrophotometer on the other side of the gelatin perhaps and taking a photo of the scatter on the gelatin.

Sandor Lab Experimentation Results 12/10/2019

HANNA RAINIERO - Dec 10, 2019, 8:18 PM CST

Title: Sandor Lab Experimentation Results

Date: 12/10/2019

Content by: Team

Present: n/a

Goals: To document the results of the 405 nm wavelength testing on photoconverting KikGR33 mouse lymph nodes.

Content:

For raw data see attached excel file.

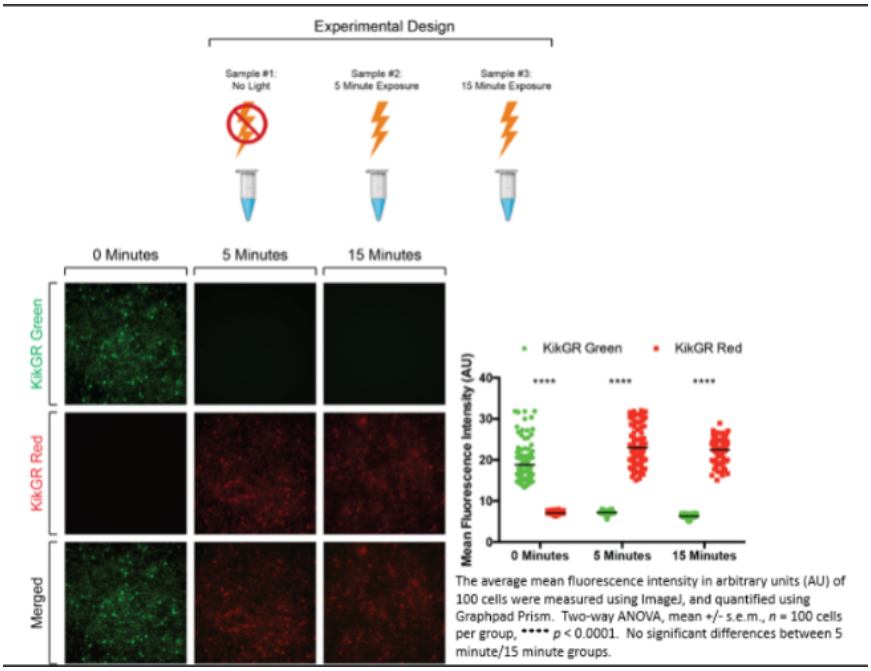


Figure 1: *Summary of the testing procedure and the results of the photoconversion.*

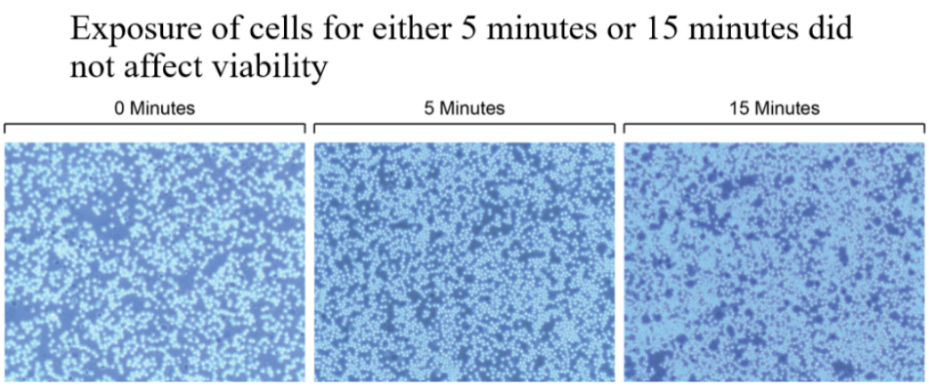
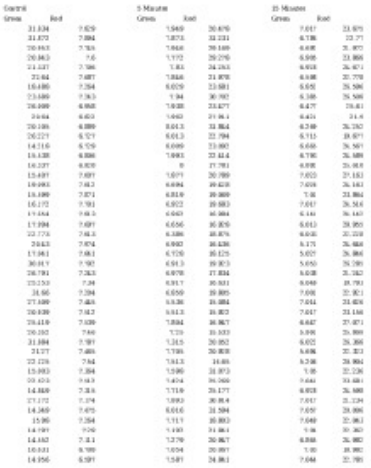


Figure 2: *Trypan blue showed that cell viability was not affected by the 405 nm LED.*

Conclusions/action items:

Martin in the Sandor Lab helped to analyze the imaging results after photoconversion. This is a summary of the primary results.

HANNA RAINIERO - Dec 10, 2019, 8:43 PM CST



KikGR_Quantitation_Melinda.xlsx(14.3 KB) - download

Temperature Testing 12/10/2019

Lisa Xiong - Dec 10, 2019, 8:46 PM CST

Title: Temperature Testing with the Breakout Boards

Date: 12/11/2019

Content by: Lisa

Present: n/a

Goals: To document the data collected from the temperature testing and the analysis.

Content:

Temperature was measured from the back of the LEDs for 5 minutes and analyzed (*VassarStats*). Change in temperature is neither statistically significant nor correlated to time for both the 405 nm and 465 nm LEDs (regression analysis, p=0.565 and p=0.187).

Table 1: *Temperature collected from the back of the 465 nm LED breakout board.*

Time (Seconds)	Temperature (°C)
30	23.1
60	23.2
90	23.1
120	23.3
150	23.2
180	23.2
210	23.2
240	23.2
270	22.5
300	23

Table 2: *Temperature collected from the back of the 405 nm LED breakout board.*

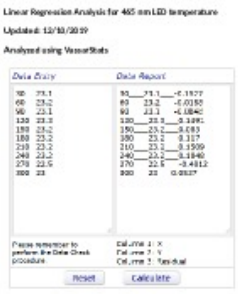
Time (Seconds)	Temperature (°C)
30	22.9
60	24.3
90	24
120	23.9
150	24
180	24
210	24
240	23.9
270	23.9
300	23.7

The regression analysis results are in the word document attached to this page.

Conclusions/action items:

Testing results showed us that temperature and heat produced from the LED is not going to be an issue.

Lisa Xiong - Dec 10, 2019, 8:53 PM CST



'

Linear_Regression_Analysis_for_465_nm_LED_temperature.docx(168.7 KB) - download Results of the VassarStats analysis. These are the screenshots of our results. VassarStats does not have an export function.

Lisa Xiong - Dec 10, 2019, 8:53 PM CST

'

Analysis_405_nm_LED.docx(170.5 KB) - download Results of the VassarStats analysis. These are the screenshots of our results. VassarStats does not have an export function.

Ocean Optics Spectrophotometer testing 12/10/2019

HANNA RAINIERO - Dec 10, 2019, 8:16 PM CST

Title: Ocean Optics Spectrophotometer Testing

Date: 12/10/2019

Content by: Hanna

Present: All

Goals: Identify Wavelength and Intensity of the LEDs to compare with our design specifications

Content:

For raw data see attached excel file and for matlab code.

For the LED intensity and wavelength testing, the data had to be further analyzed because the USB 2000+ gives a light intensity measured in counts every 100ms, and for our purposes intensity should be in units of mW/cm2. Every count of photon energy is calculated with $h * c/\lambda$ where h is Planck's constant, c is the velocity of light, and λ is the wavelength measured (Equation 1). Since the counts are measured within 100ms, the number of counts in one second is 10 times more than the counts in 100 ms. The USB2000+ has light sensitive array with 2048 pixels which is $14\mu m$ x $200\mu m$ [6]. Then, the light intensity within a certain area may be calculated by the light energy divided by the pixel area (Equation 2).

$$E = counts * \frac{1s}{100ms} * \frac{h * c}{\lambda} \qquad \textit{Equation (1)}$$

$$light\ intensity\ per\ area = \frac{E}{Area} \qquad \textit{Equation (2)}$$

By using these 2 equations, the spectrophotometer intensity data could be converted into the light intensity units specified by the client. The data was then analyzed for mean wavelength and the upper and lower bounds of photoconversion or photoactivation, mean wavelength at peak intensity, and the standard error at each to compare consistency across the LEDs (Fig. 16).

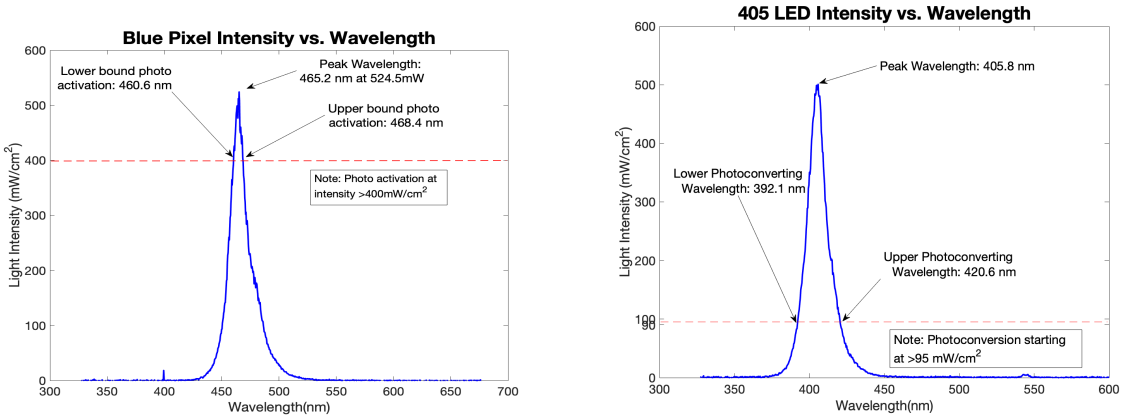
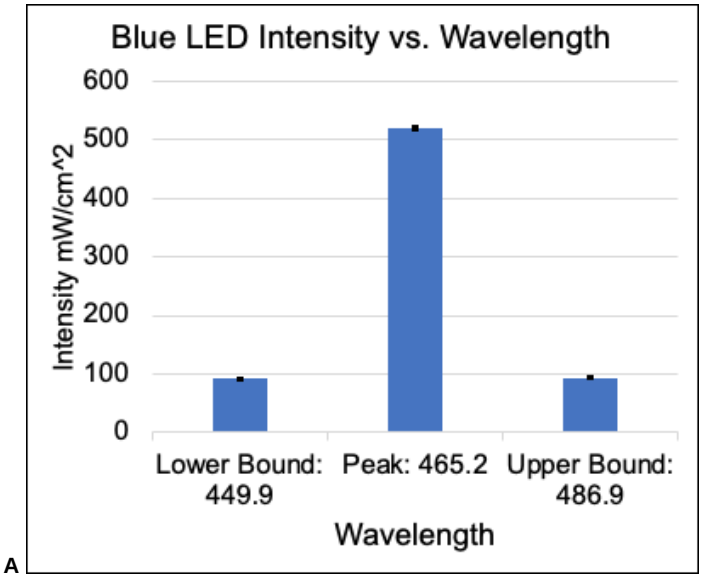


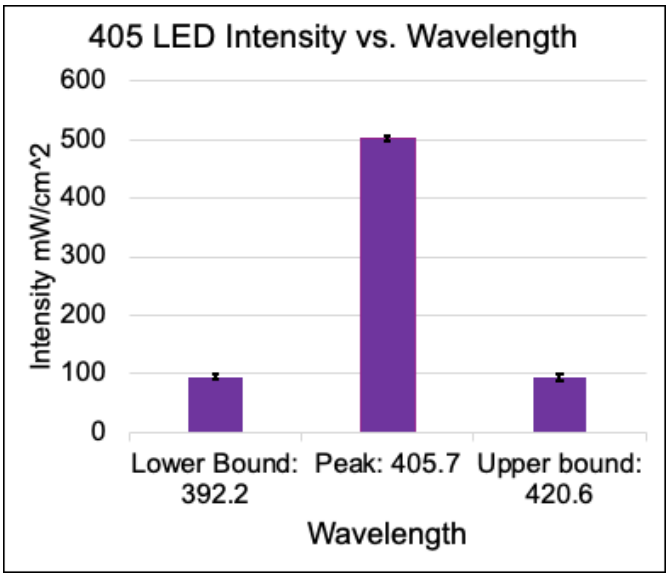
Figure 2: Wavelength vs. Intensity plots for the Neopixel (Blue Pixel) and 405 LED. The plots were analyzed using MATLAB to identify the standard error of the LEDs to ensure their consistency. Additionally, for the purposes of photoactivation and photoconversion, the mean LED wavelengths at the photoconversion upper and lower thresholds (95 mW/cm2 for 405nm and 400 mW/cm2 for 450-490 nm). Also the mean peak intensity and wavelength was assessed.

For the Blue LEDs, the mean lower bound wavelength at 400 mW/cm2 was 449.9 nm (SE=4.02x10-14 nm) and the mean upper bound wavelength was 486.9 nm (SE = 0.1 nm). The peak wavelength and intensity was 465.2 nm (SE= 0 nm) and 520.73 mW/cm2 (SE = 2.46 mW/cm2) (Fig. 17A). For the 405 nm LEDs, the mean lower bound wavelength at 95 mW/cm2 was 392.2 nm (SE=0.1

nm) and the mean upper bound wavelength was 420.6 nm (SE = $6.96x10^{-14}$ nm). The peak wavelength and intensity was 405.7 nm (SE= 0.1 nm) and 501.9 mW/cm$_2$ (SE = 1.75 mW/cm$_2$) (Fig. 17B).



A



B

Figure 3: A, Wavelength vs Intensity within the photoactivating and photoconverting intensity threshold. The Blue LED photoactivating range (400 mW/cm$_2$) is on average from 449.9 nm and 486.9 nm with a peak wavelength at 465.2 nm and intensity of 520.73 mW/cm$_2$. B, The photoconvertible range (95mW/cm$_2$) of the 405 nm LED is on average from 392.2 nm and 420.6 nm with a peak wavelength at 405.8 nm and intensity of 501.9 mW/cm$_2$.

Conclusions/action items:

With this testing we've identified that our LEDs meet the design specifications that we've outlined in our PDS and as we've learned throughout the semester, more precise specifications for each unique mouse model as outlined in our final report.

HANNA RAINIERO - Dec 10, 2019, 8:14 PM CST

Overview

Sheet 1: *405 and Blue iso*

leadmau5_matlab.xlsx(30.3 KB) - download

HANNA RAINIERO - Dec 10, 2019, 8:16 PM CST

```
file = uigetfile('.txt');
A = load(file);
reference = [470.2540,470.6100];
wavelength = A(400:1400,1);
points = A(400:1400,2);
Light_Energy = zeros(size(wavelength,1),1);

for i = 1:size(wavelength,1)
    Light_Energy(i,:) = points(i,:) * 10 * 3e8 *6.626e-34*1e9/(wavelength(i,:));
end
intensity = 1000*Light_Energy*10000/(0.025^2*pi*5*140.6*2000.6)
figure;
p = plot(wavelength,intensity,'b-','LineWidth',2);
ylabel('Light Intesity (mW/cm^2)');
xlabel('Wavelength(nm)');
title('Intensity vs. Wavelength')
```

Ledmau5.m(506 Bytes) - download

405 and 480nm LED Temperature Testing 4/27/2020

Lisa Xiong - Apr 27, 2020, 9:57 PM CDT

Title: 405 and 480nm LED temperature testing

Date: 4/27/2020

Content by: Lisa and Hanna

Present: n/a

Goals: To document the raw data that was collected when analyzing the PDMS covered LED and its affect on tap water room temperature.

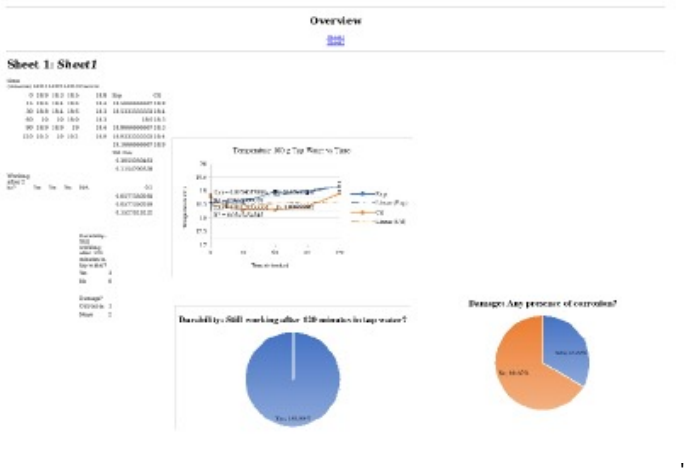
Content:

The raw data that was collected from temperature analysis is attached as an Excel file.

Conclusions/action items:

By attaching an Excel file, future groups will be able to see how we analyzed the data. If the data was imported into LabArchives it would lose the formulas and statistics associated with the data analysis.

Lisa Xiong - Apr 27, 2020, 9:57 PM CDT



UPDATED_Temperature_vs_Time.xlsx(34.1 KB) - download

Raw data for Ocean Optics Analysis 4/27/2020

Lisa Xiong - Apr 27, 2020, 10:43 PM CDT

Title: Raw data for Ocean Optics Analysis

Date: 4/27/2020

Content by: Lisa

Present: n/a

Goals: Document and store the raw data collected this semester for the wavelength, intensity, voltage, and program brightness measurements.

Content:

The two files attached contain the 405 nm data and 465 nm data (labelled as 480) collected from the Ocean Optics spectrophotometer.

1. 405 nm
    - Contains four sub-folders:
        - COATED_405nm
            - Ten replicates at maximum voltage
        - COATED_405nm_voltage-intensity
            - Three replicates at each voltage label of the subfolder
        - UNCOATED_405nm
            - Ten replicates at maximum voltage
        - UNCOATED_405nm_voltage-intensity
            - Three replicates at each voltage label of the subfolder
2. 465 nm (labelled as 480)
    - Contains four sub-folders:
        - COATED_480nm_5_brightness
            - Ten replicates at maximum voltage and 'program' brightness of 5
        - COATED_480nm_brightness-intensity
            - Three replicates at each 'program' brightness of the folder from 1 to 5. Replicate 1_b2 means that the data in this folder are three replicates for program brightness 1.
        - UNCOATED_480nm_5_brightness
            - Ten replicates at maximum voltage and 'program' brightness of 5
        - UNCOATED_480nm_brightness-intensity
            - Three replicates at each 'program' brightness of the folder from 1 to 5. Replicate 1_b2 means that the data in this folder are three replicates for program brightness 1.

Conclusions/action items:

To document RAW data that was collected from our data analysis.

Lisa Xiong - Apr 27, 2020, 10:43 PM CDT

405nm.zip(869 KB) - download

Lisa Xiong - Apr 27, 2020, 10:43 PM CDT

480nm.zip(623.6 KB) - download

Gelatin Phantom Preliminary

HANNA RAINIERO - Apr 29, 2020, 10:27 AM CDT

Title: Brain gelatin phantom testing

Date: 4/28/20

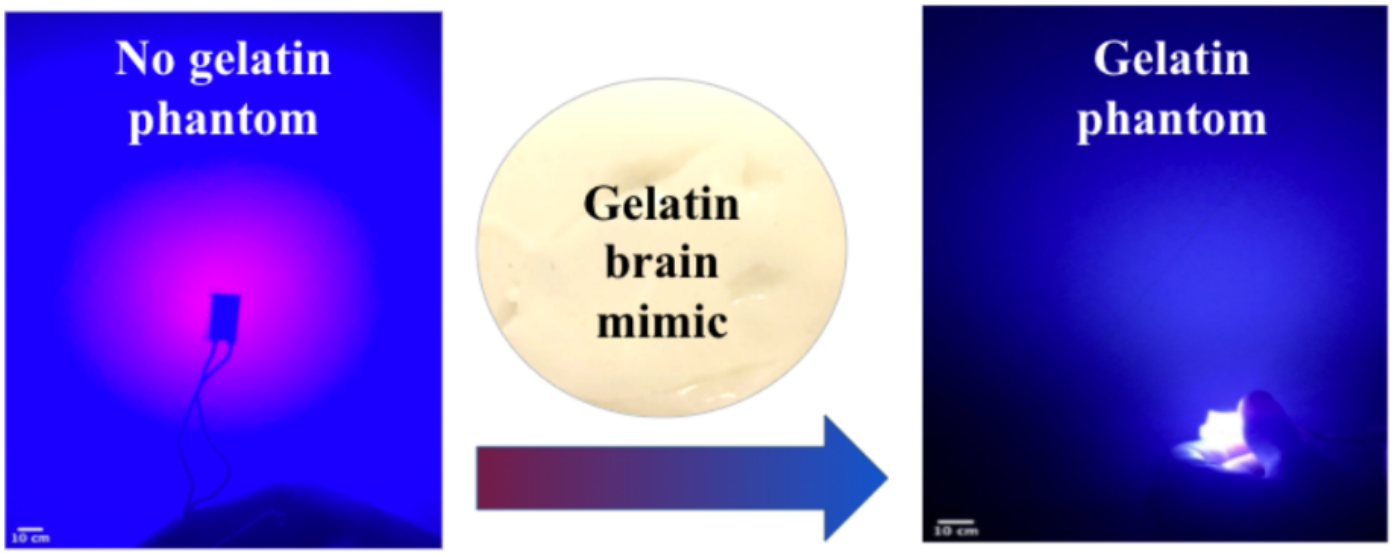
Content by: Hanna

Present: n/a

Goals: See if we can identify LED penetration/scatter effects while we are delayed from performing experiments in Dr. Sandor's Lab

Content:

A brain phantom was created from gelatin made with 50% water and 50% milk with otherwise following manufacturers' instruction. A suitable container could not be found to put the gelatin in, so the gelatin is non-uniformly 6mm thick. A significant change in the wavelength and intensity of the light could be observed qualitatively however because we were trying to split up the work, it could not be measured with the spectrophotometer. The LED was shone onto a wall in order to take a good photo with a phone of the wavelength change and diffusivity after passing through the phantom.



Conclusions/action items:

This was a good start at trying to look at the impact of lipids present in "tissue" which simulates what we would expect to happen in the brain (as good as we can with the circumstances). In the future we would like to repeat to try and get a uniform thickness and possibly try other methods to measure the scatter quantitatively.

Project Design Specifications (Uploaded 12/10/2019)

Lisa Xiong - Dec 10, 2019, 11:32 AM CST

Title: Project Design Specifications (PDS)

Date: 12/10/2019

Content by: Team

Present: n/a

Goals: Document the PDS used for this semester

Content:

Implantable Light Source Development for Optogenetic Alteration of Immune Response

BME 400 Design

Client: Matyas Sandor, PhD

Advisor: Justin Williams, PhD

Team members: Ruochen Wang, Jacky Tian, Lisa Xiong, Hanna Rainiero

Function:

The discovery of microbial opsin genes, which is a group of genes that was first studied in neurons, makes it possible to selectively control activation or silencing of neurons or other cells by light. Optogenetics is the study that combines optics with tissue genetically modified to express light-sensitive channels in the cell membrane. Our client aims to study immune trafficking in tuberculosis and inflammation of the brain by using optogenetics [1]. Our group's product will be safe to be implanted in mice and should emit light within certain wavelength requirement. The light source can also be switched on and off easily by operator for research use. The light's intensity is able to trigger all of the light sensitive channels inside the mouse tissue.

Client requirements:

The goal of our client is to use optogenetic activation or blocking of neurons to alter immune cell functions in mice to understand inflammatory responses in brain and lung diseases [1]. In vivo light delivery is key to this project and our client needs a solution for 480nm and possible 405nm light that can deliver light to a larger area, which is about one square centimeter, and can be switched on and off for specific increments in the mice. The heat produced by the light should neither be harmful nor kill the cells and tissues near implantation site. The light should be delivered deep enough to stimulate the lung tissue of the mice without causing harmful phototoxicity. The light should also be reusable if it is expensive to fabricate.

Design requirements:

1. Physical and Operational Characteristics

a. Performance requirements:

The device will be turned on for the complete duration of the experiment which will last for two hours. Not only does the device need to be powered for the duration of the experiment, it must continue to be functional and biocompatible under physiological conditions within the mouse's subcutaneous tissue (wet, temp: 36.9 °C, pH: 6-8) [2].

Light must have a size of approximately one square centimeter with a broad light source range able to penetrate deep into the organs of the mice. It also needs to have a wavelength of 405nm and/or 480nm without producing UV rays that may damage the tissue.

Light source must be able to be switched on and off for 15-30 second intervals over each 2-hour experiment. The light source must be flexible and able to be inserted subcutaneously to the mice's skull.

b. Safety:

The heat generated by light should be minimal and not be harmful to neighboring cells and tissues. The thermal tolerance for implantable devices is approximately 1 degree celsius. During the duration of the experiment, the device should be able to diffuse the heat from the light emitting diode to prevent thermal damage. In addition, the team should make sure the UV light is not produced by the light source as the UV light would cause harm to the cells. The device should also be designed to limit phototoxicity of the living tissue. The material should also be biocompatible so that it will not cause an inflammatory response in the tissue. Electronic components of the device will be coated in a biocompatible and implantable material (example parylene C or PDMS) to prevent voltages and currents from harming the mice.

c. Accuracy and Reliability:

The light needs to be durable and biocompatible so that it is able to withstand the environment inside the blood vessels of mice. Also, the light source developed should be broad enough to cover enough areas on the organs of the mice to make sure the light-sensitive genes can be triggered and monitored. The light emitting diodes should emit wavelengths of 405nm and 480nm.

-

d. Life in Service:

Ideally the electrical components of the device will be reusable while the coating biomaterial would be covering the light and could be sterilized by ethanol. The light source should also work continuously and consistently without unpredicted damage in the hardware. The heat sink would also aid performance in maintaining the energy from dissipating in the form of heat to maintain light intensity for the time during use.

e. Operating Environment:

The device will be exposed to physiological conditions in the subcutaneous tissue of the mice in the chest and cranium. The device will be exposed to the body temperature and pH of the mice which is approximately 36.9 °C and pH 6-7, respectively [2]. Since the device is in an aqueous, saline environment, there is risk of corrosion and/or electric shock. The individuals at risk are the mouse itself or the person carrying out the experiment and this risk must be mitigated.

f. Ergonomics:

The device should be readily and easily picked up using tweezers. Once the device is in the mouse, it will not be handled by a human until it needs to be removed - a microcontroller will simply need to be turned on to operate the device.

g. Aesthetics, Appearance, and Finish:

The design needs to be small, compact, and streamlined. Since the design will be used in vivo, wires are acceptable but not preferred. The materials used need to be durable and able to function when in the subcutaneous environment of the mice. The device needs to be biocompatible and prevent any form of liquid from seeping into the device.

2. Production Characteristics

a. Target Product Cost:

The client did not specify the budget as long as we make reasonable use of the money provided by our client. Our team will try to minimize the amount we might spend and try to make our device reusable and reliable.

3. Miscellaneous

a. Standards and Specifications: FDA Regulation of Implantable Medical Devices

Our device to be built will be implanted subcutaneously in the mouse. According to the FDA the ambient temperature must not increase by more than 1°C or brain damage may occur [3].

b. Customer:

For a preliminary design specification in regard to customer, the device should be user-friendly (easy to handle, will not fall apart easily when mishandled, etc). This device will not be available to the commercial consumer - it will be used for research purposes at the client's research lab.

c. Patient-related concerns:

Our design will not be applied to patients directly even though the ultimate goal might be to alter immune response of humans. For our research subjects, mice, the use of light source must not be detrimental to the research projects and the device should be safe to mice when being implanted.

d. Competition:

1. Biocompatible optical fiber-based nerve cuff can be used for light delivery that wraps around the target neuron. The research mainly considers light delivery to peripheral axons [3].
2. Epidural fiber-optic implants: Epidural fiber is used in light delivery for spinal cords. The system [4] enables sufficient light intensity and different light wavelength to be delivered.

References:

[1] Fabry, Z., Chreiber, HS., Harris, MG., Sandor, M. (2008). Sensing the microenvironment of the central nervous system: immune cells in the central nervous system and their pharmacological manipulation. Curr Opin Pharm. doi: 10.1016/j.coph.2008.07.009.

[2] The Staff of the Jackson Laboratory. Biology of the Laboratory Mouse. New York: Dover Publications INC., 1966.

[3] Reichert, W. (2008). Indwelling Neural Implants: Strategies for Contending With the in Vivo Environment (Frontiers in neuroengineering). CRC Press, Chapter 3.

[4] Towne, C., Montgomery, K. L., Iyer, S. M., Deisseroth, K., & Delp, S. L. (2013). Optogenetic Control of Targeted Peripheral Axons in Freely Moving Animals. PLoS ONE,8(8). doi:10.1371/journal.pone.0072691

[5] Bonin, R. P., Wang, F., Desrochers-Couture, M., Ga¸secka, A., Boulanger, M., Côté, D. C., & Koninck, Y. D. (2016). Epidural optogenetics for controlled analgesia. Molecular Pain,12, 174480691662905. doi:10.1177/1744806916629051

Conclusions/action items:

This is a copy of the PDS that we wrote in Google Docs.

2/3/2020 UV time and dose kinetics

HANNA RAINIERO - Feb 03, 2020, 5:31 PM CST

HANNA RAINIERO - Feb 03, 2020, 5:38 PM CST

Title: UV time and dose kinetics

Date: 2/3/2020

Content by: Hanna

Present: Hanna

Goals: Identify lethal dosing of UV radiation to maintain viability of our cells and prepare testing

Content:

Based on the two attached papers we should collect for flow cytometry analysis ~ 24 hours following UV radiation. In terms of the lethal dose we need to calculate the J/cm^2 for our device to compare our device to those used in the papers however it's important to note that in the papers attached the wavelength is ~300 nm while ours is 400nm so it might be up to us to collect our own data with different brightnesses and durations to find a time and dose optimized for photoconversion and cell viability.

Conclusions/action items:

Determine energy output of our LEDs (potentiometer?). Talk with Matyas and Martin about doing in vitro viability study with cells irradiated at different intensities and durations.

HANNA RAINIERO - Feb 03, 2020, 5:38 PM CST

Flow cytometric quantification of UV-induced cell death in a human squamous cell carcinoma-derived cell line: dose and kinetic studies

'

UV_induced_cell_death.pdf(5.3 MB) - download

HANNA RAINIERO - Feb 03, 2020, 5:38 PM CST

View Article Online / Journal Homepage / Table of Contents for this issue

PAPER www.rsc.org/pps | Photochemical & Photobiological Sciences

Photobiological and thermal effects of photoactivating UVA light doses on cell cultures

Julianne Foreman,[a] Marilyn Dietrich[b] and W. Todd Monroe*[a]

Received 20th November 2006, Accepted 9th January 2007
First published as an Advance Article on the web 6th February 2007
DOI: 10.1039/b616879a

While near-ultraviolet light has been widely used to photoactivate fluorophores and caged compounds in cells, little is known of the long-term biological effects of this light. UVA (315–400 nm) photoactivating light has been used in hundreds of studies to observe cell dynamics and is now being employed in higher doses to control longer-duration photosystems (e.g. gene expression). Assays for VC_5-propidium iodide apoptosis flow cytometry assays were used to determine responses of HeLa cells to doses of UVA light up to 23.83 J cm^{-2}. Cells seeded at low densities had higher percentages of apoptosis and necrosis and were also more susceptible to UVA damage than cells seeded at higher densities. The dose to induce apoptosis and death in 50% of the cells (dose$_{50}$) was determined for two different commercially available UVA light sources: 7.6 J cm^{-2} for the GreenSpot photocuring system and 2.92 J cm^{-2} for the BlakRay lamp. All BlakRay doses tested had significant cellular responses, whereas no significant cellular responses were found for doses below 1.6 J cm^{-2} from the GreenSpot light source. A temperature-controlled microscope stage system was used to determine direct heating from the UVA sources and also the effect that cooling cell cultures during photoexposure has on minimizing cell damage. Cooling during the BlakRay photoexposure significantly reduced the percentage of necrotic cells, but there was no significant difference for cooling during photoactivation with the GreenSpot. Differences in cell responses to similar UVA doses of different intensities suggest that photodetection should be considered along with total dose and thermal conditions in photoactivation studies.

Introduction

UVA light (315–400 nm) has been widely used to photoactivate fluorophores and photochemicals in live cells. Short, intense exposures of these wavelengths have also been commonly used to activate caged compounds. Caged compounds have a synthetically attached group that renders the target molecule inert and is released upon light exposure in order to restore activity of the target molecule; one classic example includes caged ATP that has a single cage that blocks bioactivity.[1,2] Photocage chromophores are now being used to control activities of larger biomolecules, such as proteins and nucleic acids, which contain more attached cages per target molecule, therefore necessitating increased light doses to achieve recovery of activity.[3,4] In contrast to classic photolysis experiments that study fast kinetic responses (e.g. ATP activity), relatively longer-term studies of gene expression and metabolic pathways require evaluation of cell health several days after photoexposure. Biological effects, including apoptosis, photoinactivation, chromosomal damage, and cellular response to UV-induced DNA lesions, have been used to reveal sub-photobiological cellular findings.[5]

Ultraviolet radiation consists of three ranges: UVA (315–400 nm), UVB (280–315 nm), and UVC (180–280 nm). UVC and UVB are known to induce the p53 pathway, whereas the role of UVA depends very specifically on cell type and is not as clear.[5] The toxicity of a UVA photon has been described as "one thousand times smaller than that of a UVC photon and about one hundred times smaller than that of a UVB photon".[5] Ultraviolet radiation affects various cellular targets including DNA, cell surface receptors, kinases, phosphatases, and transcription factors.[6] The biological effects, including mediator release, altered surface receptors, and apoptosis induction of UV radiation, occur when a cellular chromophore absorbs UV radiation and transduces the energy into a biochemical signal.[6] Apoptosis, a known response to UV irradiation, is a programmed cell death during which the cell undergoes very specific biochemical and morphological events. The apoptotic cascade of events includes condensing chromatin, cell shrinkage and blebbing, loss of asymmetry of the plasma membrane and the formation of apoptotic bodies, which are eventually engulfed via phagocytosis without causing inflammation.[6] Some studies are beginning to look at genes involved in UVA-induced apoptosis, but the exact pathway has yet to be clearly defined.[6] It has been proposed that the mechanism of biological effects of UVA radiation involves absorption by a non-DNA chromophore, which causes the generation of oxygen species or the upregulation of critical target molecules.[11]

In addition to the photophysical effects of UV photons, temperature conditions have been found to play a role in cellular apoptotic effects that counter existing photoexposure studies. Previous studies have found that cooling HeLa cells to below the transition temperature of the membrane (15°C–10°C) prevents receptor clustering and is associated with reduced apoptosis caused by UVB.[14] While several studies done the chilling and incubation during UVA exposure, specific justifications for cooling are not detailed.[15,16] To

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[b]Department of Veterinary Pathology, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA, USA

Photobiological_effects_of_UVA.pdf(366.7 KB) - download

2/10/20 Previous Publications on Implantable LEDs

HANNA RAINIERO - Feb 26, 2020, 12:32 AM CST

Title: Previous Literature on Implantable LEDs

Date: 2/10/20

Content by: Hanna

Present: Hanna

Goals: Identify previous literature in the area we are planning on publishing

Content:

See paper attached. It appears there is a similar methods with implantable LEDs within optogenetics research. Multi Channel Systems manufactures an implantable LED for optogenetics research to stimulate channel rhodopsin. I had difficulty finding the device on their site however the paper mentions a wireless implantable LED made by them.

Conclusions/action items:

This paper is valuable in identifying specifications that we need to outline. It is also important to note that we are bringing optogenetic tools and models to immunology and immunologically based diseases so that is our niche when we go to seek publication.

HANNA RAINIERO - Feb 26, 2020, 12:32 AM CST

frontiers in INTEGRATIVE NEUROSCIENCE

TECHNOLOGY REPORT ARTICLE

A wirelessly controlled implantable LED system for deep brain optogenetic stimulation

Mark A. Reed, Vince Gu, Tracy Mapley, Quanhai Fu, James Mackie and Henry H. Yin

fnint-09-00008.pdf(3 MB) - download

2/16/20 Sandor Research

HANNA RAINIERO - Feb 26, 2020, 12:40 AM CST

Title: Application of our 465 nm LED

Date: 02/16/20

Content by: Hanna

Present: Hanna

Goals: Identify the impact of our 465 LED and how it will be used

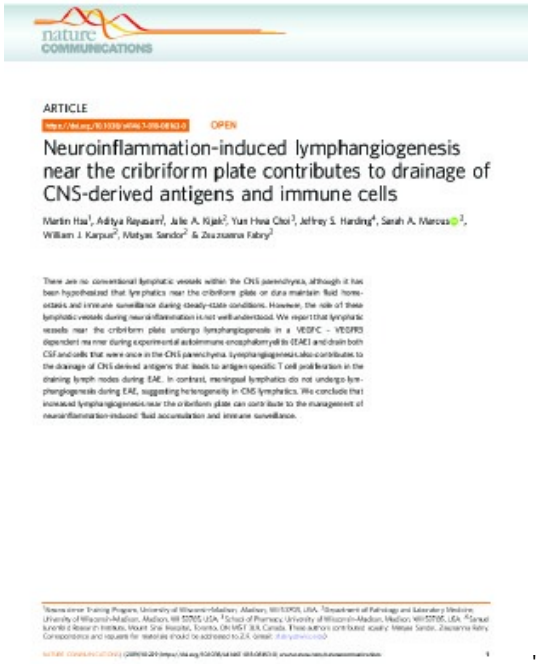
Content:

See paper attached. The CNS is often thought to be immune privileged with limited immune cell infiltration. Dr. Sandor's lab identified immune infiltration and draining across the cribiform plate in mouse models. With this key information our implantable LED may serve to activate dendritic cells with channelrhodopsin in their membrane in the brain and their migration to the lymph outside of the brain may be found as they pass through the plate to nearby lymph nodes.

Conclusions/action items:

Our 465 nm LED will be used to activate dendritic cells in the brain which may then migrate to surrounding lymph nodes by passing through the cribiform plate.

HANNA RAINIERO - Feb 26, 2020, 12:40 AM CST



nature COMMUNICATIONS

ARTICLE

OPEN

Neuroinflammation-induced lymphangiogenesis near the cribriform plate contributes to drainage of CNS-derived antigens and immune cells

Martin Hsu[1], Aditya Rayasam[2], Julie A. Kijak[2], Yun Hwa Choi[3], Jeffrey S. Harding[4], Sarah A. Marcus[2], William J. Karpus[2], Matyas Sandor[2] & Zsuzsanna Fabry[3]

sandor_paper.pdf(7.9 MB) - download

PCB Coatings

HANNA RAINIERO - Apr 29, 2020, 10:41 AM CDT

Title: Learning more about PCB coatings

Date: 4/29/20

Content by: Hanna

Present: n/a

Goals: Learn more about PCB coatings

Content:

I read a blog discussing different methods of coating a device as we have little understanding of the terminology making it difficult to find the appropriate coating that we need.

Based on this source, it sounds like we will want to do what is called potting which will fully encapsulate our device however we need to ensure the material is non-conductive, thermally diffusive, and had good binding to the PCB (the last we had issues with PDMS). The page also talks about parylene C which would be the most desirable coating for our device however current facilities are unable to provide this to us.

https://blog.paryleneconformalcoating.com/how-to-choose-between-potting-and-conformal-coating

Another paper I read that has a chronically implanted optogenetic brain implant uses EPO-TEK® H20E - Epoxy Technology which is an electrically conductive epoxy that may be useful if we decide to go with a flexible PCB design. However because it is electrically conductive it will need a nonconductive coating over it. In the paper they first coated the electronic components of their device with a clear epoxy then added PDMS via spin coating which may be a better option to help us overcome some of the issues we were seeing with our PDMS coating.

link to paper: https://www.frontiersin.org/articles/10.3389/fnins.2019.00819/full

Link to datasheet for epoxy: http://www.epotek.com/site/administrator/components/com_products/assets/files/Style_Uploads/H20E.pdf

Conclusions/action items:

For our device, we may want to try either a potting technique with epoxy or try the epoxy + spin coating PDMS mentioned in the paper.

Design Matrices

HANNA RAINIERO - Oct 08, 2019, 7:16 PM CDT

HANNA RAINIERO - Oct 08, 2019, 7:18 PM CDT

Title: Design Matrices

Date: 10/8/2019

Content by: Hanna

Present: All

Goals: Identify our final design using a design matrix of weighted criteria

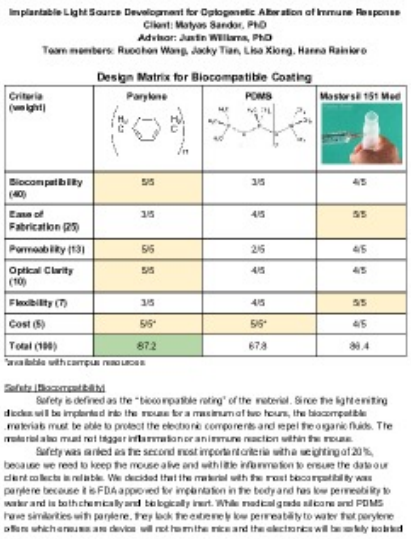
Content:

See attached. Our final design is LEDs integrated into a PCB coated with Parylene.

Conclusions/action items:

We will fabricate a prototype of the PCB integrated LEDs and coat it with Parylene C for testing

HANNA RAINIERO - Oct 08, 2019, 7:19 PM CDT



Implantable Light Source Development for Optogenetic Alteration of Immune Response
Client: Matyas Sandor, PhD
Advisor: Justin Williams, PhD
Team members: Ruochen Wang, Jacky Tian, Lisa Xiong, Hanna Rainiero

Design Matrix for Biocompatible Coating

Criteria (weight)	Parylene	PDMS	Mastersil 151 Med
Biocompatibility (40)	5/5	3/5	4/5
Ease of Fabrication (25)	3/5	4/5	5/5
Permeability (13)	5/5	2/5	4/5
Optical Clarity (10)	5/5	4/5	4/5
Flexibility (7)	3/5	4/5	5/5
Cost (5)	5/5*	5/5*	4/5
Total (100)	87.2	67.8	88.4

*available with campus resources

Safety (Biocompatibility)

Safety is defined as the "biocompatible rating" of the material. Since the light-emitting diodes will be implanted into the mouse for a maximum of two hours, the biocompatible materials must be able to protect the electronic components and repel the organic fluids. The material also must not trigger inflammation or an immune reaction within the mouse.

Safety was ranked as the second most important criteria with a weighting of 20%, because we need to keep the mouse alive and with little inflammation to ensure the data our client collects is reliable. We decided that the material with the most biocompatibility was parylene because it is FDA approved for implantation in the body and has low permeability to water and is both chemically and biologically inert. While medical grade silicone and PDMS have similarities with parylene, they lack the extremely low permeability to water that parylene offers which ensures are device will not harm the mice and the electronics will be safely isolated

NEW_DESIGN_MATRIX.pdf(450.4 KB) - **download**

In Vitro Experimental Design

HANNA RAINIERO - Apr 29, 2020, 11:26 AM CDT

Title: Exp Planning for In Vitro

Date: 4/29/20

Content by: Hanna

Present: N/A

Goals: plan out some in vitro experiments

Content:

Create and array with different intensities and different times to expose cells to light

Materials: glass dishes, appropriate media, positive control for apoptosis (TNF-a or something like that), note that we could try photoconverting on TCPS however it may autofluoresce. Ideally three replicates per group with analysis via flow cytometry.

intensities calculated from Ocean Optics Spectrophotometry Data:

x = voltage

y = intensity

y = 2,873.3x - 8257 (line is a somewhat rough fit)

	Exposure time (ideally <1mm away)				
Voltage/Intensity	1 min	2 min	3 min	4 min	5 min
2.9 V/75 mW/cm^2	3	3	3	3	3
2.91V/100mW/cm^2*	3	3	3	3	3
2.94 V/ 200 mW/cm^2	3	3	3	3	3
2.97 V/300 mW/cm^2	3	3	3	3	3

*95 mw/cm^2 cited as needed for photoconversion

Because we want triplicates of everything it might be easier to have smaller dishes though this might be something we will discuss with the Sandor Lab.

after 24 hours, flow cytometry

FS-A/SC-A to gate out schmutz

FS-A/FS-H to select single cells

to find green cells: excitation 488 nm emision 517 nm

to find red cells: excitation 594 nm emission 593 nm

to find dead cells: ghost or propidium iodide or DAPI

Conclusions/action items:

Here is a tentative *in vitro* experimental assay plan with a goal of finding the appropriate wavelength and time to optimize photoconversion and minimize phototoxicity through optimizing time of exposure and intensity of exposure.

Optogenetics 09/06/19

Jacky Tian - Oct 09, 2019, 2:19 PM CDT

Title: Concepts in Optogenetics

Date: 09/06/2019

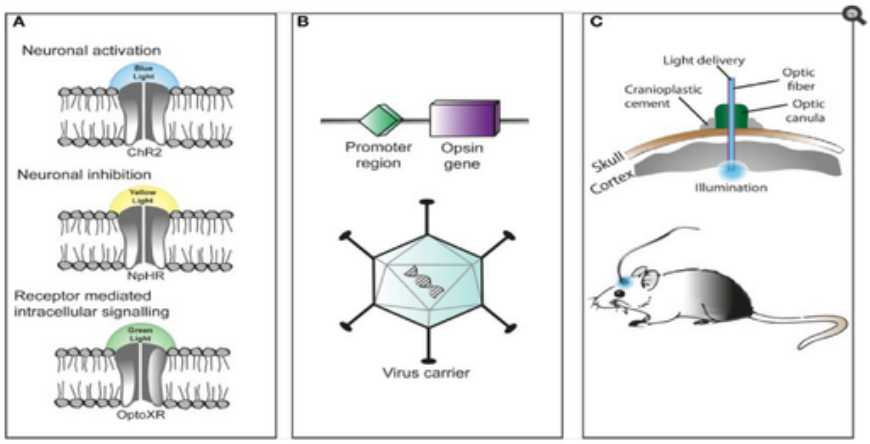
Content by: Jacky Tian

Present: Jacky Tian

Goals: Clarify certain concepts in optogenetics

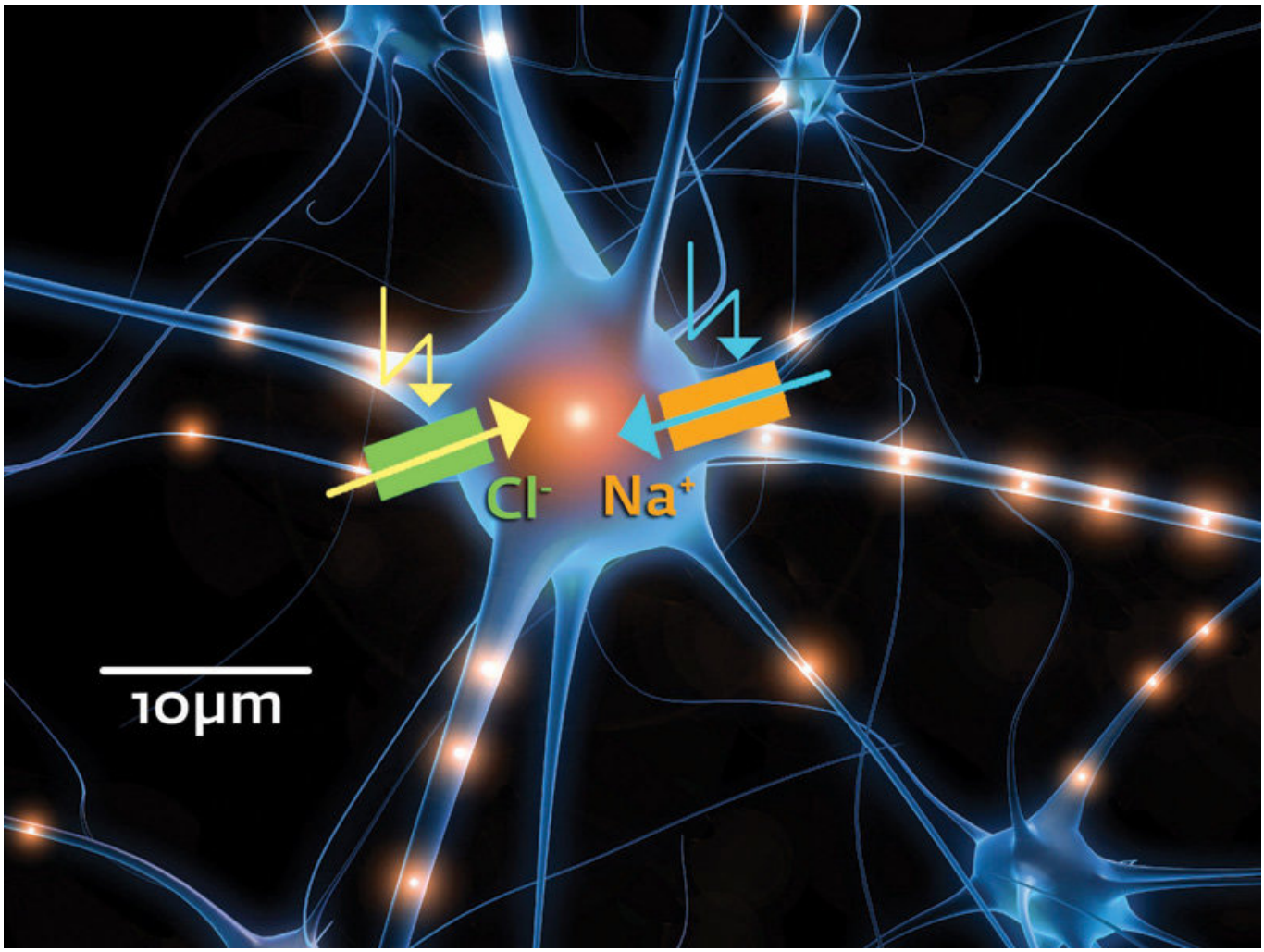
Content: Optogenetics is a biological technique that involves the use of light to control cells in living tissue, typically neurons, that have been genetically modified to express light-sensitive ion channels. It is a neuromodulation method that uses a combination of techniques from optics and genetics to control and monitor the activities of individual neurons in living tissue—even within freely-moving animals—and to precisely measure these manipulation effects in real-time.The key reagents used in optogenetics are light-sensitive proteins.

Figure 1



Three primary components in the application of optogenetics are as follows (A)Identification or synthesis of a light-sensitive protein (opsin) such as channelrhodopsin-2 (ChR2), halorhodopsin (NpHR), etc... (B) The design of a system to introduce the genetic material containing the opsin into cells for protein expression such as application of Cre recombinase or an adeno-associated-virus (C) application of light emitting instruments.

Shown above is an example using concepts in optogenetics to solve real-life problem.



At a basic level, the nervous system can be thought of as a highly complex electrical circuit. Every neuron contains a variety of pump and channel proteins that control the flow of ions across its membrane, maintaining a negative membrane potential in the resting neuron. Activation signals, for example from neurotransmitters, cause positively-charged ions to flow into the cell from the external environment via these channel proteins, resulting in membrane depolarization. At a certain threshold, this triggers an action potential — a rapid influx of sodium ions that effectively reverses the voltage inside the cell, initiating a chain reaction of sodium-ion influx that propagates down the length of the axon, eventually causing the release of neurotransmitters that stimulate or inhibit the production of electrical impulses in neighboring neurons.

Background (Imported from BME 300)

Jacky Tian - Dec 09, 2019, 11:11 PM CST

Title: Background Research and Project Introduction (Imported from **BME 300**)

Date: 09/09/2019

Content by: Jacky Tian

Present: Jacky Tian

Goals: Get clearer about the project and the client's expectation. In addition, write the introduction and background part of the preliminary report

Content:

Tuberculosis(TB) is a potentially serious infectious disease that mainly affects the lungs. Even though most infections do not have symptoms, about 10% of those latent infections progress to active disease which kills about half of those infected[1]. For the ultimate goal which is to cure tuberculosis in human, lots of research projects have been carried out to find ways to alter immune cell functions in mice to understand inflammatory responses in brain and lung diseases. Currently, researchers are using mice as models since they are easy to handle and their genetic, biological and behavior characteristics closely resemble those of human. A widely used technique to alter immune response is optogenetics which can control and monitor the activities of individual neurons in living tissue-even within freely-moving animals-and to precisely measure the manipulation effects in real-time[1]. Dr. Sandor and his lab members from Department of Pathology & Laboratory Medicine,University of Wisconsin-Madison, are currently using fiber optic photo conversion to observe the behavior immune cells on lungs when mice are infected with tuberculosis. The lab is currently using a light with a wavelength of 405nm to 470nm that converts granulomas from dyed green to red and is doing research on how many green immune cells have moved in. By doing this, they can observe how the body responds to inflammation caused by tuberculosis. The lab has already developed light-sensitive genes but the light delivered to the lungs is not sufficient enough to trigger the genes due to several restraints such as light intensity, areas that the light can reach, and the depth the light can penetrate.

Over the past two decades, numerous optical stimulation tools have been developed but they are hard to be employed into vivo applications since these tools are mainly based on either the utilization of exogenous cofactors or the expression of multiple proteins. Optogenetics is an emerging neuromodulation technique that can render neurons controllable by light. This technique combines optical and genetic methods to activate or inhibit specific neurons[2].

Nowadays, there is an increasing need to construct novel optogenetic implants by using appropriate engineering approaches. These implants should be able to achieve precise light emission, and to reliably deliver light to targeted areas. Besides, the implants should be capable of being applied for multi-site (area) and multi-layer (depth) operations so that the light intensity can reach the threshold.

Our client, Dr. Sandor’s lab is interested in doing research on photoconversion of kikGR33 Mice. The Mycobacterium Tuberculosis (Mtb) Crimson infection will last for approximately four weeks. Then, twenty minutes of lighting on left lung is needed to photoconvert the immune cells. After 1 and 7 days of incubation, the photoconverted granuloma from the left lung will be examined and those immune cells will appear red if the immune response has been altered.

The lab is currently using approximately 1000mW 405 nm light. Since light is pivotal in the photoconversion process, a few fiber optic cable adjustments have been already made such as the increased conversion area by a higher NA (numerical aperture from 0.22 to 0.4) to increase the cone of emission from 25° to 45° and the increased output intensity by increased cable width (from 0.69 to 0.87 mm) and decreased exposed fiber. However, the current method utilized by Dr. Sandor’s Lab is still not optimal because not all slices have photoconversion sites and not all 5 photoconversion sites can be found. As demonstrated in the presentation of Dr. Sandor’s Lab, the potential causes include 1) the light is not immediately adjacent to lung tissue so it may not reach inner slices 2) ribs or other tissues may block some signals. 3) mice may move enough that site is not efficiently exposed for the full time. 4) bleeding/bruising is observed occasionally which may obscure the light. To solve these problems, our team will design a light emitting device that can deliver light at appropriate wavelength sufficiently and effectively to alter the immune response.

Reference:

[1] "Tuberculosis Fact sheet N°104". WHO. October 2015. Archived from the original on 23 August 2012. Retrieved 11 February 2016.

[2] H. Zhao, “Recent Progress of Development of Optogenetic Implantable Neural Probes,” International Journal of Molecular Sciences, vol. 18, no. 8, p. 1751, Nov. 2017.

Implantable Connectors 11/13/2019

Jacky Tian - Dec 09, 2019, 11:20 PM CST

Title: Research existing implantable connectors after talk w. Dr. Amit Nimunkar

Date: 11/13/2019

Content by: Jacky Tian

Present: Jacky Tian

Content: Definition of electrical connector from Wikipedia: An electrical connector is an electromechanical device used to join electrical terminations and create an electric circuit. Most electrical connectors have a gender – i.e. the male component, called a plug, connects to the female component, or socket. The connection may be removable (as for portable equipment), require a tool for assembly and removal, or serve as a permanent electrical joint between two points.

Useful links: https://www.hermeticsolutions.com/resources/hermetic-connector-models-drawings

https://iopscience.iop.org/article/10.1088/1741-2552/ab36df/pdf

LED Measurement on Ocean Optics 10/29/2019

Jacky Tian - Dec 10, 2019, 12:50 AM CST

Title: Research on Ocean Optics Website

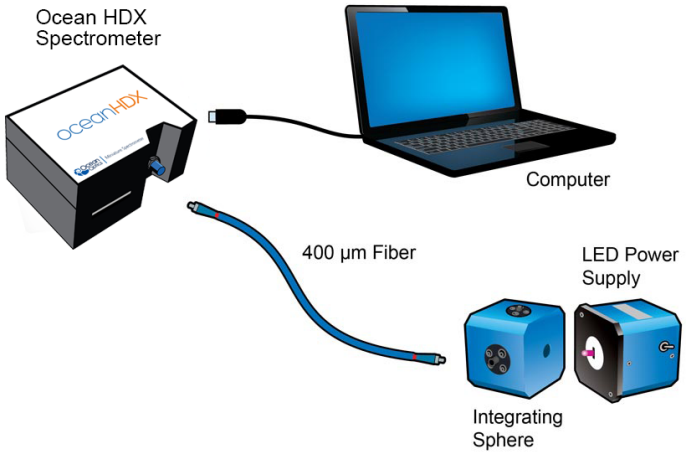
Date: 10/29/2019

Content by: Jacky Tian

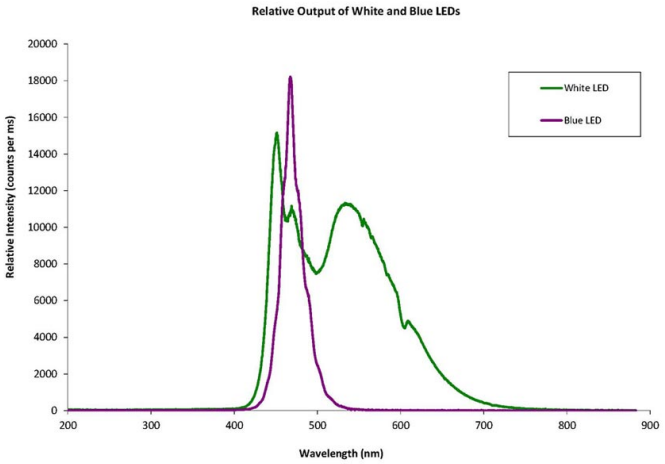
Present: Jacky Tian

Content: Link to the website: https://oceanoptics.com/application/led-measurement/

LED Measurement: Ocean Optics Spectrometer and accessories can be configured to measure absolute or relative irradiance of LEDs and other radiant sources, with a variety of optical fixtures, calibrated sources and other tools for convenient measurements. Use our components and software to determine absolute spectral intensity values (in watts, joules, lumens or candela), color parameters (including X, Y, Z and L*, a*, b*), and features such as dominant wavelength, peak wavelength, centroid and FWHM. Also, setups can be integrated into LED testing and binning machines for quality control in LED manufacturing, helping to ensure consistency in spectral output and color.



Example Setup:



Spectrometers can be configured to measure the relative or absolute spectral output of LEDs.

Jacky Tian - Dec 10, 2019, 12:51 AM CST

Ocean Optics

Application Note

Keywords

- LEDs
- Color
- Color rendering index
- Spectral output

Techniques

- Emissive color measurement
- Irradiance

Applications

- LED measurement
- CCT determination
- CRI measurement

Miniature Spectrometers Address Challenges of LED Research and Production

Written by Hartle Mobley, PhD

Thanks to the evolution of small, handheld spectrometers, applications such as the testing and binning of LEDs are more easily managed than with previous instruments. Indeed, spectrometers can be deployed to measure LED emission wavelengths as well as brightness and power output. To appreciate why miniature spectrometers are viable tools for LED measurement, it helps to understand the typical performance parameters being measured.

Color and Spectral Output of LEDs

Although determining the correlated color temperature (CCT) of incandescent light sources is fairly simple, as these spectra fit nicely on a blackbody radiator curve, doing the same for fluorescent and LED light sources is much more challenging. Those sources have very different spectral shapes, making it harder to perform an accurate fit using traditional color filter-based instruments.

The simplest color meters use diodes or pixels covered by red, green and blue filters. More advanced systems use tristimulus filters. These types of systems work quite well for incandescent light sources but struggle to provide accurate answers for light sources such as LEDs. To detect small color changes, very high color resolution is necessary – resolution a spectrometer can achieve. A spectrometer captures the light reflected, transmitted or emitted by a sample and uses a dispersing element to split it into discrete wavelengths, capturing the spectral data for the sample under test. Because the instrument captures the complete spectral power distribution rather than merely measuring power in observer-specific wavelength bands, the resulting color measurement is more precise and robust. There has been much debate on how much wavelength resolution is needed to make an accurate color measurement, with competing resolution standards from CIE (International Commission on Illumination) and ASTM (American Society for Testing and Materials) varying from 1 nm to 20 nm.

App-Note-Miniature-Spectrometers-Address-Challenges-of-LED-Research-and-Production.pdf(637.1 KB) - download

FDA Regulation on Implants 11/20/2019

Jacky Tian - Dec 10, 2019, 1:10 AM CST

Title: Research FDA Regulations on implants

Date: 11/20/2019

Content by: Jacky Tian

Present: Jacky Tian

Content: FDA Regulation on Implants (Copied from its website):

Medical implants are devices or tissues that are placed inside or on the surface of the body. Many implants are prosthetics, intended to replace missing body parts. Other implants deliver medication, monitor body functions, or provide support to organs and tissues.

Some implants are made from skin, bone or other body tissues. Others are made from metal, plastic, ceramic or other materials.

Implants can be placed permanently or they can be removed once they are no longer needed. For example, stents or hip implants are intended to be permanent. But chemotherapy ports or screws to repair broken bones can be removed when they no longer needed.

The risks of medical implants include surgical risks during placement or removal, infection, and implant failure. Some people also have reactions to the materials used in implants.

All surgical procedures have risks. These include bruising at the surgical site, pain, swelling and redness. When your implant is inserted or removed, you should expect these types of complications.

Infections are common. Most come from skin contamination at the time of surgery. If you get an infection, you may need to have a drain inserted near the implant, take medication, or even have the implant removed.

Over time, your implant could move, break, or stop working properly. If this happens, you may require additional surgery to repair or replace the implant.

If you learn that you need a medical implant, you should ask your doctor the following questions before agreeing to the procedure:

- Will my implant be permanent or removable? If the device is permanent, find out how long it should last. If the device is removable, find out how long it will be implanted in you and what factors will determine when it can come out.
- What material will the implant be made from? Make sure you are not allergic to any of the components in the implant.
- How many of these procedures have you done? The more experience a doctor has with inserting implants, the better the outcome may be.
- What are the complication rates from the procedure? Make sure you understand the risks of the surgery, infection, and device failure.
- What are the benefits of the procedure? Make sure you understand how the device will benefit you and if it will affect your quality of life.

Temperature Testing (Coagulation Damage) 11/28/2019

Jacky Tian - Dec 10, 2019, 3:54 AM CST

Title: Temperature Testing (Coagulation Damage)

Date: 11/28/2019

Content by: Jacky Tian

Present: Jacky Tian

Goals: Research the temperature that will lead to coagulation damage so that we will test our device and see whether the temperature measured exceeds the threshold.

Content: The temperature of our device should not exceed **50°C.**

link to the paper: https://onlinelibrary.wiley.com/doi/abs/10.1002/%28SICI%291096-9101%281999%2925%3A3%3C257%3A%3AAID-LSM10%3E3.0.CO%3B2-V?sid=nlm%3Apubmed

Background

Interstitial laser coagulation (ILC) is a method of local tissue destruction for solid tumors such as irresectable hepatic metastases from colorectal cancer. With the availability of new magnetic resonance (MR) techniques, which allow real time tissue temperature mapping, it is essential to know the critical temperature and exposure times leading to cell death.

Materials and Methods/Study Design

Samples (8 mm3) of solid rat tumor (CC-531, syngenic to the WAG/Rij rat strain), were warmed in tubes for four different temperatures (40, 50, 60 or 80°C) and four different exposure times (3, 6, 12, or 24 minutes). Combinations were replicated in five-fold. Cell viability was assessed with three methods: Trypan blue exclusion test in collagenase/dispase dissociated samples, NADH activity in snap frozen samples and outgrowth for 2 weeks under the renal capsule of WAG/Rij rats.

Results

Results of the three methods revealed that viability was not affected with heating at 40 and 50°C except for 24 minutes at 50°C. At higher temperatures cell death occurred at all exposure times.

Conclusion

The temperature range resulting in sufficient tissue coagulation for cell death is between 50°C and 60°C for a short duration (<3 minutes). These data can be used to achieve complete tumor destruction and minimal surrounding tissue damage during real-time MR-controlled ILC

Recommended Temperature Change Specified by AAMI 12/01/2019

Jacky Tian - Dec 10, 2019, 3:26 AM CST

Title: Recommended Temperature Change Specified by AAMI

Date: 12/01/2019

Content by: Jacky Tian

Present: Jacky Tian

Goals: Research the recommended temperature change brought by implanted medical devices specified by the American Association of Medical Instrumentation (AAMI)

Content: In implantable medical devices, the effects of a chronic temperature increase should be within the range of 1 celcius degree to 2 celcius degrees. This number is the limit recommended by the American Association of Medical Instrumentation (AAMI) for implantable medical devices. The amount of power that can be dissipated by the body and still remain within this limit is a question of great importance.

Link to the detailed discussion: https://www.ncbi.nlm.nih.gov/pubmed/21204399

02/03/2020 Flex Circuits Material

Jacky Tian - Feb 26, 2020, 3:15 PM CST

Title: Flex Circuits Material

Date: 02/03/2020

Content by: Jacky Tian

Goals: Figure out what material our team should look at

Content:

While most standard PCBs have a fiberglass or metal base, flex circuit cores consist of a flexible polymer. The majority of flex PCBs have a polyimide (PI) film as a substrate. PI film does not soften when heated, but it stays flexible after thermosetting. Many thermosetting resins like PI become rigid after heating, making PI a superior material in flex PCB construction. Standard PI film does not have good resistance to humidity and tears, but choosing upgraded PI film mitigates these issues.

A flex PCB also requires an adhesive or special base material for its layers to attach. Manufacturers previously used adhesives only, but this method reduced the PCB’s reliability. To resolve these issues, they developed adhesiveless PI that attaches to copper without an adhesive. This material allows for thinner designs with a lower risk of via breakage. Instead of using a solder mask to cover and protect a flex circuit, manufacturers use a coverlay film also created with PI. If you want the area on the flex pcb to be rigid, the manufacture can laminate a stiffer to that portion, but the signal cannot travel between the flex and the stiffer.

Wireless Power 09/12/19

Jacky Tian - Oct 09, 2019, 2:19 PM CDT

Title: Wirelessly Powered Internal Optogenetics in Mice

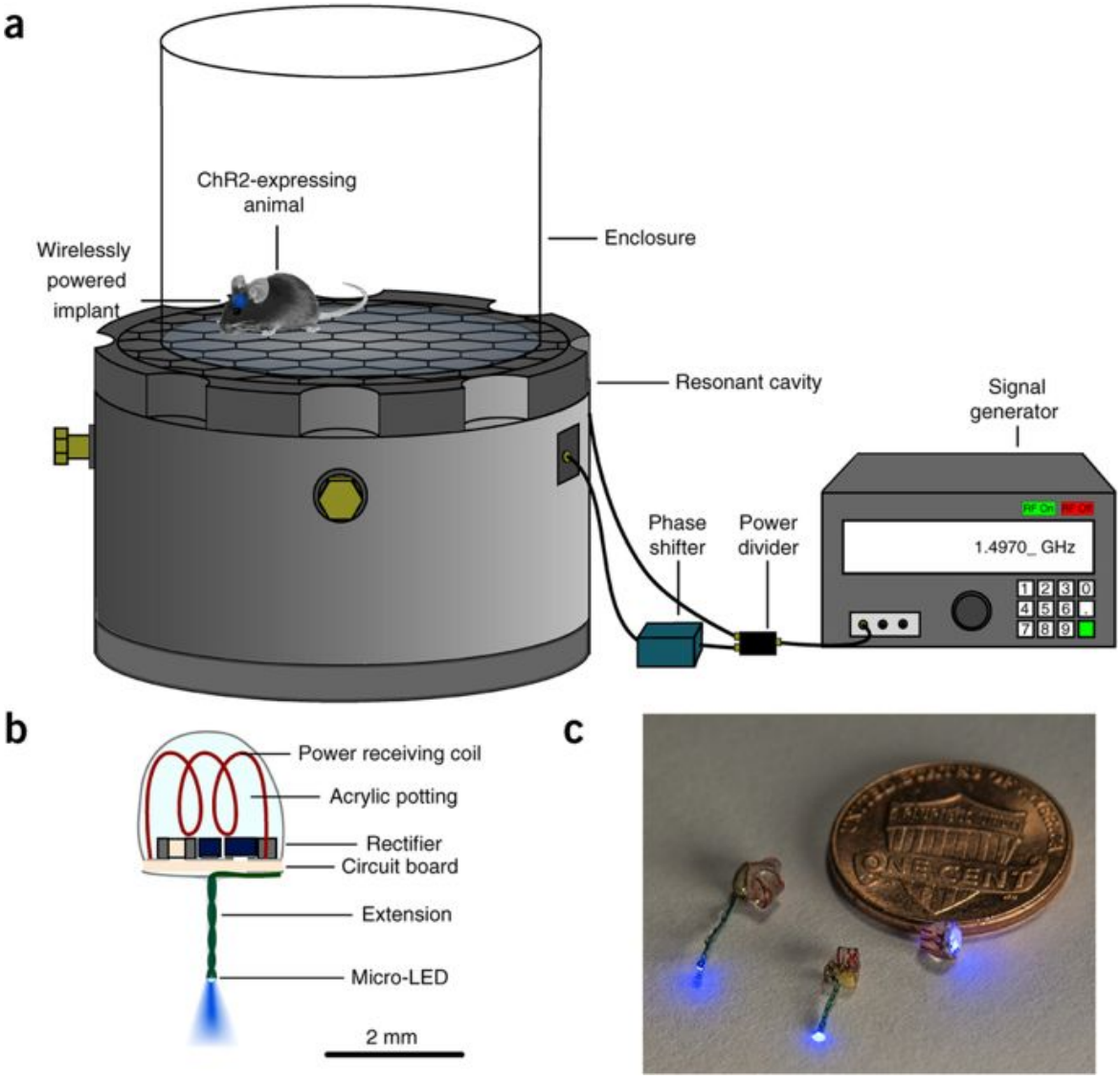
Date: 09/12/2019

Content by: Jacky Tian

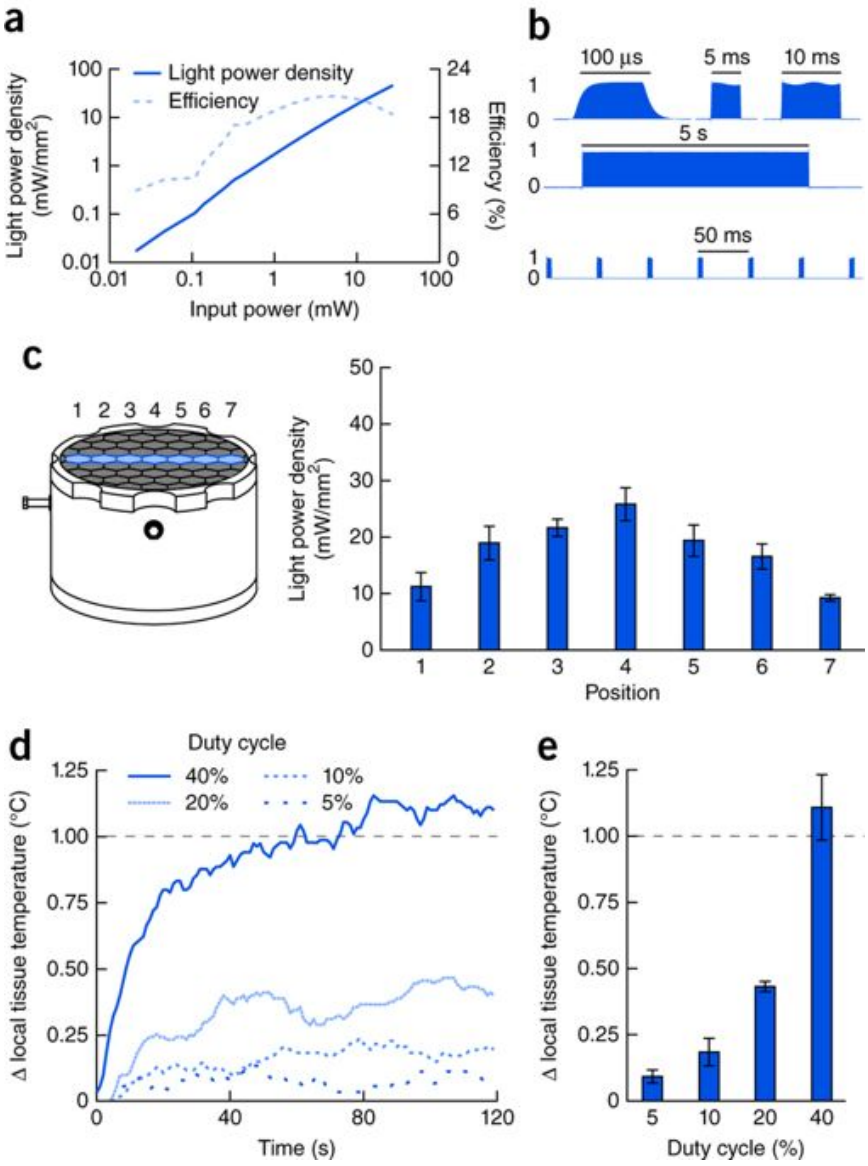
Present: Jacky Tian & Ruochen Wang

Goals: Look at current designs and see whether those designs can shed light on ours.

Content:



(a) Diagram of light-delivery system. (b) Schematic of wireless implant customized for the brain. (c) Size comparison of wireless implants (left to right: peripheral nerve endings, brain, spinal cord) with a US 1-cent coin.



(a) Light power density and efficiency of the LED are each a function of the power supplied to the micro-LED; here, we powered the LED with a wired circuit (not wirelessly). (b) Fidelity of light output for step-function pulses of various pulse widths. Relative transient intensities (arbitrary units) for 100-µs, 5-ms, 10-ms and 5-s pulses, as well as consecutive 5-ms pulses are shown. (c) Calculated light power density across the width of the behavioral area above the resonant cavity. (d,e) Local heating of tissue directly adjacent to the LED. A wired LED probe is inserted into brain with a light power density of 20 mW/mm2 at 5%, 10%, 20% and 40% duty cycles (5-ms pulse width; 10-Hz, 20-Hz, 40-Hz and 80-Hz frequencies, respectively; n = 3 technical trials). Dashed lines denote the temperature associated with neural damage. (d) Temperature versus time; each trace is an average of three trials. (e) Average of final 30 s of light delivery. Bar graphs show mean ± s.e.m.

Specific design ideas can be found in this link: https://www.nature.com/articles/nmeth.3536

Reference:

Montgomery, K., Yeh, A., Ho, J., Tsao, V., Mohan Iyer, S., Grosenick, L., Ferenczi, E., Tanabe, Y., Deisseroth, K., Delp, S. and Poon, A. (2015). Wirelessly powered, fully internal optogenetics for brain, spinal and peripheral circuits in mice. Nature Methods, 12(10), pp.969-974.

Battery Free 09/12/19

Jacky Tian - Oct 09, 2019, 2:19 PM CDT

Title: Fully implantable optoelectronic systems for battery-free

Date: 09//12/2019

Content by: Jacky Tian

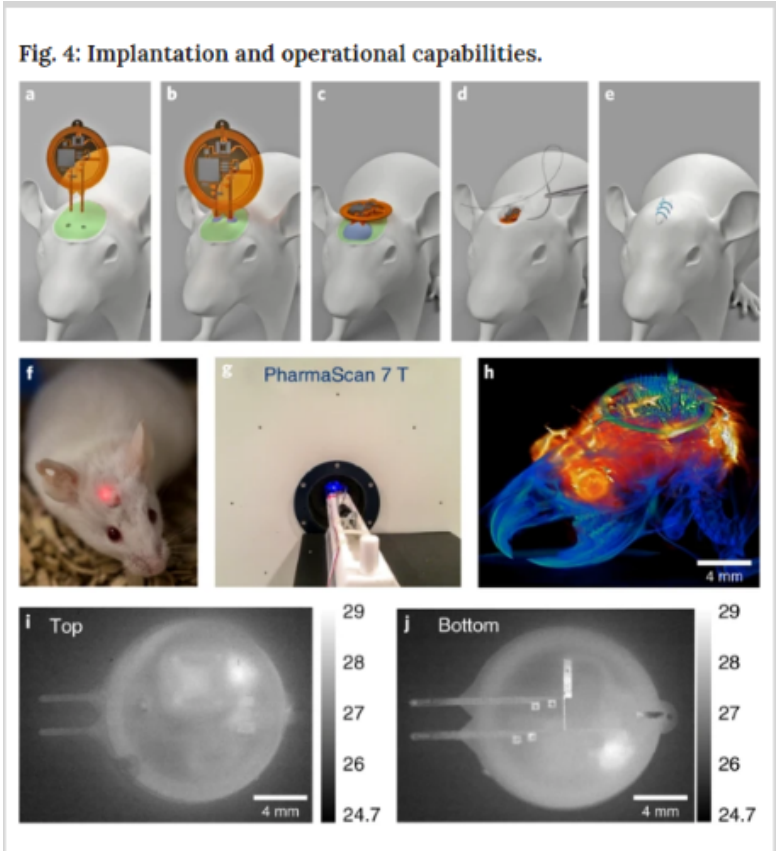
Present: Jacky Tian

Content:

Abstract of this paper: Recently developed small, fully implantable devices for optogenetic neuromodulation eliminate the physical tethers associated with conventional set-ups and avoid the bulky head-stages and batteries found in alternative wireless technologies. The resulting systems allow behavioral studies without motion constraints and enable experiments in a range of environments and contexts, such as social interactions. However, these devices are purely passive in their electronic design, thereby precluding any form of active control or programmability; independent operation of multiple devices, or of multiple active components in a single device, is, in particular, impossible. Here we report optoelectronic systems that, through developments in integrated circuit and antenna design, provide low-power operation, and position- and angle-independent wireless power harvesting, with full user-programmability over individual devices and collections of them. Furthermore, these integrated platforms have sizes and weights that are not significantly larger than those of previous, passive systems. Our results qualitatively expand options in output stabilization, intensity control and multimodal operation, with broad potential applications in neuroscience research and, in particular, the precise dissection of neural circuit function during unconstrained behavioral studies.

Figure 1: Digitally controlled multimodal optogenetic implants

This image cannot be copied. Labels: a,b, Layered view (a) and electrical schematic (b) of a power regulated system with minimal footprint. c,d, Layered view (c) and electrical schematic (d) of an advanced bilateral system with four individually controlled light sources in a multi μ-ILED device. e,f, Layered view (e) and electrical schematic (f) of the programmable intensity device. Electrical components for panels b, d and f: blue LED symbol, μ-ILED; red LED symbol, red indicator LED; Schottky diode symbol, RF Schottky diode; capacitor symbols, ceramic capacitors. g, Photographic image of the regulated implantable device. h, Photographic image of the programmable multi μ-ILED device. i, Photographic image of the programmable intensity device.



a–e, Step-by-step surgical procedure for the implantation of the programmable bilateral multi μ-ILED device. Green coloured sections indicate the skull and blue coloured sections indicate cyanoacrylate and dental cement glue. f, Photograph of a mouse two weeks after surgery. g, Implant operating in an MRI scanner. h, Combined image analysis with MRI and CT results superimposed in a 3D rendering of the animal implanted with the programmable bilateral multi μ-ILED device. i, Thermal image of the top of an operating bilateral device set to 25% duty cycle on all four μ-ILEDs. j, Thermal image of the bottom of an operating bilateral device set to 25% duty cycle on all four μ-ILEDs.

Link to this paper: https://www.nature.com/articles/s41928-018-0175-0?utm_campaign=MultipleJournals_USG_DEVICE&utm_source=Nature_community&utm_medium=Community_sites&utm_content=BenJoh-Nature-MultipleJournals-Engineering-Global

Research on Biomaterial 10/1/19

Jacky Tian - Oct 09, 2019, 2:17 PM CDT

Title: Biomaterials Search

Date: 10/1/2019

Content by: Ruochen & Jacky

Present: Jacky& Ruochen

Goals: Browse all the materials that could be used

Content:

Paper: Advances in Materials for Recent Low-Profile Implantable Bioelectronics

Materials	Properties	Device Component	Applications
PDMS	Low modulus, high dielectric strength, low chemical reactivity	Microfluidic channel	Pressure monitoring
		Dielectric layer	Pressure and oxygen sensor in blood
		Substrate layer	Physiological recording
Medical grade silicone	High tear strength and elasticity, transparency	Encapsulation layer	Soft contact lens sensor, intracranial and blood pressure monitoring
Parylene C	Chemical and biological inert, low water permeability and absorption	Structural diaphragm	Intraocular pressure monitoring
		Substrate layer	Neural electrode probe, hydrocephalus shunt occlusion detection
Polyimide	High heat resistance	Substrate layer	Intraocular and cardiovascular pressure monitoring
		Structural diaphragm	Intraocular pressure monitoring
PVDF	Piezoelectricity	Structural diaphragm	Intracranial and endovascular pressure monitoring
LCP	Low dielectric constant and low moisture absorption rate	Substrate	Intraocular pressure monitoring
		Encapsulation	Active intraocular pressure monitoring

Linked to this paper: https://www.mdpi.com/1996-1944/11/4/522/htm

Conclusions/action items:

PDMS, Parylene C and polyimide are all potentially usable biomaterials. High dielectric strength is desirable and optical properties need to be examined. It seems they all have ok optical properties for the project.

Pulse-width Modulation 09/30/19

Jacky Tian - Oct 09, 2019, 2:07 PM CDT

Title: Research on pulse-width modulation

Date: 09/30/2019

Content by: Jacky Tian

Present: Jacky Tian

Content:

Link to this paper: https://ieeexplore.ieee.org/document/7546908

Pulse width modulation (PWM), or pulse-duration modulation (PDM), is a method of reducing the average power delivered by an electrical signal, by effectively chopping it up into discrete parts. The average value of voltage (and current) fed to the load is controlled by turning the switch between supply and load on and off at a fast rate. The longer the switch is on compared to the off periods, the higher the total power supplied to the load.

This paper shows that pulse-width modulation (PWM) of the intensity of a light-emitting diode (LED) can enable control of photo-stimulation intensity equivalent to direct amplitude modulation. This result has significant implications for fully implantable light delivery tools, as PWM can be implemented with simple and miniaturized circuit architectures. The authors have modified a telemeter device previously developed by our group to include a small form-factor LED capable of generating sufficient optical power with manageable electrical power requirements and minimal heat generation. The authors have tested key device components in an in vitro mouse brain slice preparation and shown that pulse-width-modulation is an alternative method to modulate photo-stimulation intensity using a miniature circuit and providing easy control.

Yokogawa Device 12/07/19

Jacky Tian - Dec 09, 2019, 10:31 PM CST

Title: Existing device for optogenetics research (Yokogawa)

Date: 12/07/2019

Content by: Jacky Tian

Present: Jacky Tian

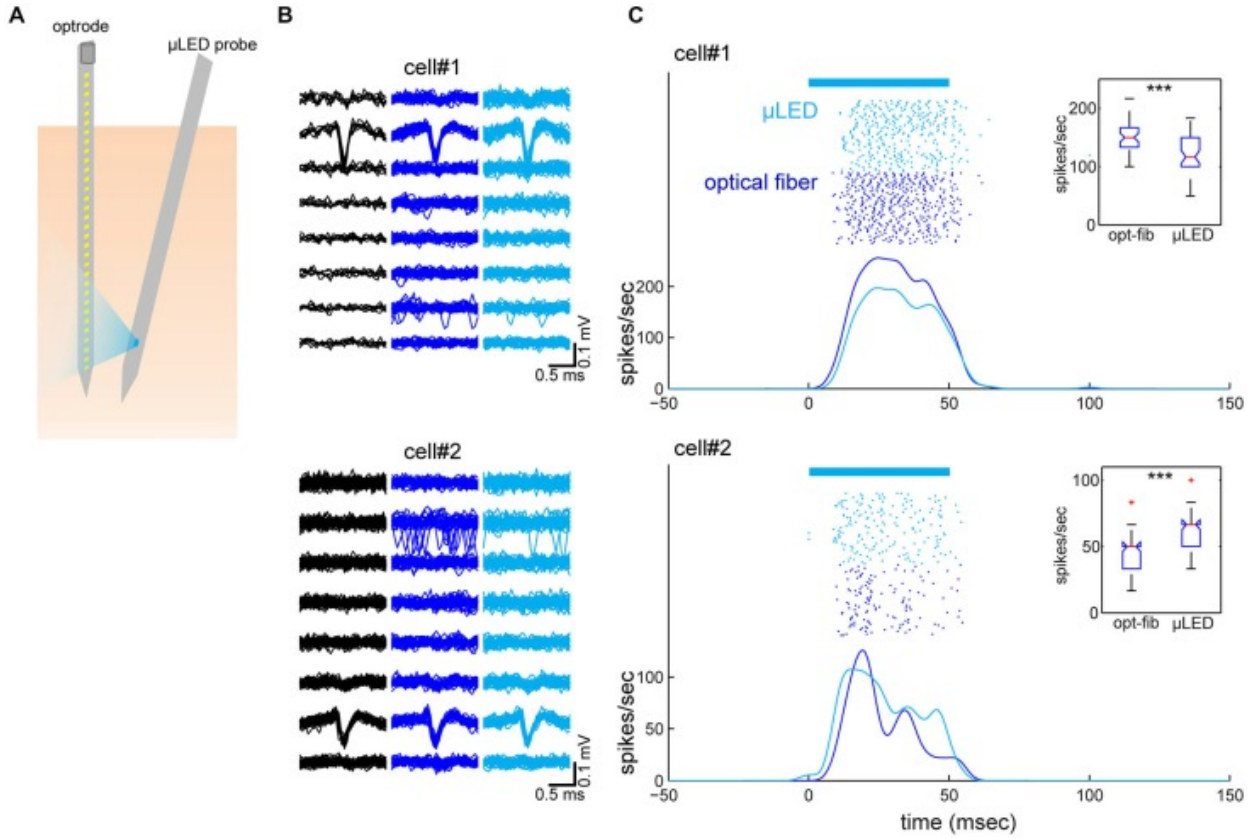
Content: Title of the published paper: "Optogenetic activation of neocortical neurons *in vivo* with a sapphire-based micro-scale LED probe"

Link to the paper: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4448043/

Abstract: Optogenetics has proven to be a revolutionary technology in neuroscience and has advanced continuously over the past decade. However, optical stimulation technologies for in vivo need to be developed to match the advances in genetics and biochemistry that have driven this field. In particular, conventional approaches for in vivo optical illumination have a limitation on the achievable spatio-temporal resolution. Here we utilize a sapphire-based microscale gallium nitride light-emitting diode (μLED) probe to activate neocortical neurons in vivo. The probes were designed to contain independently controllable multiple μLEDs, emitting at 450 nm wavelength with an irradiance of up to 2 W/mm2. Monte-Carlo stimulations predicted that optical stimulation using a μLED can modulate neural activity within a localized region. To validate this prediction, we tested this probe in the mouse neocortex that expressed channelrhodopsin-2 (ChR2) and compared the results with optical stimulation through a fiber at the cortical surface. We confirmed that both approaches reliably induced action potentials in cortical neurons and that the μLED probe evoked strong responses in deep neurons. Due to the possibility to integrate many optical stimulation sites onto a single shank, the μLED probe is thus a promising approach to control neurons locally in vivo.

Electrophysiology and Optical Stimulation

For electrophysiological recording, broadband signals were amplified relative to a cerebellar bone screw and were digitized at 20 kHz (PXI, National Instruments). Once spiking activity was detected, optical pulses were delivered from either the optical fiber or μLED to assess whether neurons could be activated by optical stimulation, after which recording sessions were initiated. Each recording session typically consisted of a non-stimulation period (up to 2 min), optrode and μLED stimulation periods (up to 3 min) and another non-stimulation period (up to 2 min). The μLED was driven by a current source (**Yokogawa**, Source Measure Unit GS610) from 0.1 mA up to 6 mA. The μLED was supplied with 4 mA (40 mW/mm2) current pulses. The light source of the optrode was a commercial GaN LED (450 nm, PlexBright, Plexon) with 58.9 mW/mm2 output at tip of the probe. This light level was used as standard for all cortical experiments as it allow for stimulation along the full length of the optrode



Simultaneously recorded neocortical neurons and their optical responses. (A) Schematic of the geometry of probe insertion into the neocortex. (B) Depth profiles of average spike waveforms of isolated single units. Signals from the bottom 8 channels are shown. Black, spontaneous activity. Blue, optical fiber stimulation. Light Blue, µLED stimulation. (C) Raster plots and peri-stimulus time histograms (PSTHs) for optically evoked responses. Fifty optical stimulation pulses, each 50 ms in duration were applied at a 2 Hz repetition rate, for both µLED (4 mA) (light blue) and fiber (58.9 mW/mm2) (blue) activation. The bar on the top indicates the timing of optical stimulation. PSTHs were smoothed by a 3-ms Gaussian kernel. Insets are boxplots of optically evoked responses for each condition and each cell (0–60 ms window from stimulus onset). ***$p < 0.001$ (two-sample t-test).

Cover the Implant with Gelatin 04/23/2020

Jacky Tian - Apr 29, 2020, 1:02 PM CDT

Title: PDMS recipe provided by Dr. Megan McClean

Date: 04/23/2020

Content by: Jacky Tian

Present: Jacky Tian

Content: There is a research paper published about how the gelatin-covered electrode implants cause less damage to brain tissue than electrodes with no gelatin coating. Very interesting paper. May be something to think about in the future for this project.

Links to paper: https://www.sciencedaily.com/releases/2017/11/171106100131.htm

Printed Circuit Board 09/20/19

Jacky Tian - Oct 09, 2019, 2:20 PM CDT

Title: Printed Circuit Board as an alternative to hand-solder

Date: 09/20/2019

Content by: Jacky Tian

Present: Jacky Tian

Content:

Definition: A printed circuit board is an electrical circuit whose components and conductors are contained within a mechanical structure. Conductive features include copper traces, pads, heat sinks, or conductive planes. The mechanical structure is made with insulating material laminated between layers of conductive material. The overall structure is plated and covered with nonconductive solder mask and silk screen to legend electronic component location.

By drawing circuits on PCB, our team can effectively get rid of wires which will make our device very easy to manipulate. Currently, there are four wires connected to each LED and each implant will have 16 wires. PCB will connect the LEDs on the board without wire connections.

Here is the link to how to draw the layout of the PCB: **http://www.circuitbasics.com/make-custom-pcb/**

Before PCB design, it's a good idea to make a schematic of the circuit. The schematic will serve as a blueprint for laying out the traces and placing the components on the PCB. Plus, the PCB editing software can import all of the components, footprints, and wires into the PCB file, which will make the design process easier.

PCB Design is usually done by converting the circuit's schematic diagram into a PCB layout using PCB layout software. There are many cool open source software packages for PCB layout creation and design.

including:

1. Autodesk Eagle
2. **PCBWizard**

Connection in Series 09/27/19

Jacky Tian - Oct 09, 2019, 2:20 PM CDT

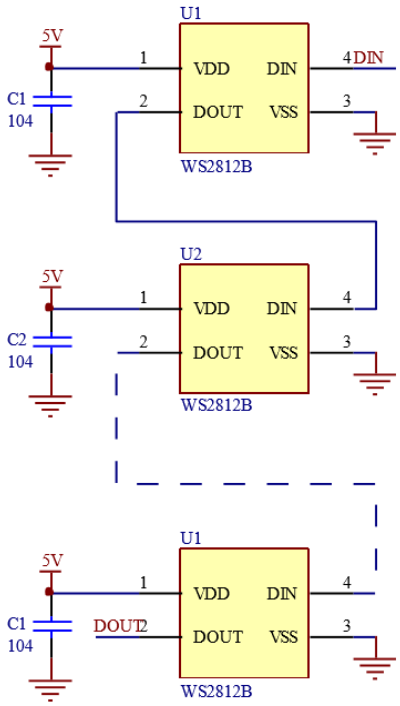
Title: Connect four LEDs in series with each other

Date: 09/27/2019

Content by: Jacky Tian

Present: Team

Content: By connecting the LEDs in series, we can ensure that the current passing through individual LED remains the same, having the potential to solve the problem that only 3 out of 4 LEDs were working properly in our previous testing. Also, even if the LEDs are connected in series, the voltage drop won't significantly affect the power of each LED.



The typical application circuit shown above is several 480nm LEDs connected in series. If there is a DIN, DOUT will be connected to DIN of the next LED and so on so forth. Pin 1 and Pin 3 as shown in the figure will be connected to the power and be grounded. By doing this, our team can reduce the amount of wires.

This circuit schematic is acquired from the data sheet of the 480nm LEDs our team purchased. Link: https://cdn-shop.adafruit.com/product-files/1138/SK6812+LED+datasheet+.pdf

Our team agreed on this connection method and we would draw the circuit on PCB soon.

PDMS Recipe 11/01/2019

Jacky Tian - Dec 10, 2019, 4:02 AM CST

Title: PDMS recipe provided by Dr. Megan McClean

Date: 11/01/2019

Content by: Jacky Tian

Present: Jacky Tian

Content:

Materials

- Slygard 184 Silicon Elastromer (Ellsworth Adhesives)
- 4” petri dishes (for storing chips)
- Small ~6” pieces of the intramedic tubing (ID 0.86mm OD 1.27mm)
- Razor blades
- Biopsy Punches (1.2mm, 1.0mm, 0.75mm diameters) (
- Nitrile gloves
- Stainless steel blunt needle, 16 ½” gauge
- Small green needle (21 ½ gauge Becton-Dickinson)
- Scotch tape
- 1ml syringes with Luer-Lok tips
- 1.5mm Coverslips
- Oven set to 65°C
- TMCS (chlorotrimethyl silane)
- plastic forks for mixing PDMS
- plastic beakers for mixing PDMS
- Vacumn jar for degassing PDMS

Protocol

Wear nitrile gloves, as oils from your hands can prevent the PDMS from curing and/or bonding properly. Please try to not drip PDMS everywhere. It is extremely hard to clean up. Don't get uncured PDMS onto cured chips, as this will prevent the chips from properly bonding to the glass coverslip. In practive this means you should use one pair of gloves for mixing the PDMS and another, clean pair for cutting out the chips and bonding them to the coverslip.

Mixing PDMS to fill the mold

1. Mix PDMS in a 1:9 ratio (by weight) curing agent to polymer in a plastic solo cup. The easiest way to do this is by weighing out the polymer first in the plastic solo cup on a balance and then adding the appropriate amount of curing agent
2. For these molds you will need ~60 g of total solution the first time you fill up the petri dish (assuming a 4" dish).
3. Mix the PDMS THOROUGHLY using a plastic fork. When you think that you’ve mixed it enough, mix it some more. Uneven mixing will lead to uneven curing of the PDMS.

Degassing the PDMS

1. Place your PDMS in the vacumn bell jar in the hood and turn on the vacumn. Please wait for your classmates because you will all need to be degassing PDMS at the same time.
2. Watch the PDMS degassing. If it looks like it is about to bubble over, release the vacumn, let the bubbles collapse, and then restart the vacumn. Keep an eye on it for at least 10 minutes.
3. Make sure that your PDMS is completely free of bubbles. The total degassing process will probably take 15 minutes. While you are waiting you may move on to testing the chips you made previously.

Pour the PDMS

1. Pour the PDMS carefully into your mold, trying hard not to introduce bubbles that you have worked so hard to eliminate.
2. If you do introduce bubbles carefully use a 21G 1 1/2 gauge needle to move them to the side.

Curing the PDMS

1. Cure the PDMS at 65°C until it is firm and not tacky at all. This will probably take an hour. You can also do this overnight if you are running out of time.

Cutting out the Chip

1. Using a razor blade, carefully cut around the mask components visible through the PDMS. DO NOT CUT YOURSELF. DO NOT under ANY circumstances push down on the underlying silicon wafer. This will crack the wafer rendering it useless for classmates and for future chip making. It is expensive to replace these molds, so BE GENTLE!!! The best way to cut out the PDMS is to gently circle, removing slightly more PDMS each time. When you see an air bubble form under the PDMS you are getting close, but DO NOT rush at this point. Carefully keep circling the groove until the chunk of PDMS pops-out.
2. Cut the large piece of PDMS into individual chips. You want each chip to fit onto your coverslip. Don't cut your chip too small, as this will give it less surface area with which to bond to the coverslip. When you have cut out your chip, cover the channel side with scotch tape.

Punch inlet and outlet ports in your chip

Blunt Needle Technique

Place a piece of scrap PDMS flat on your bench and push a blunt needle through the PDMS. Then use a smaller 21 G 1 ½ needle (pointed) to remove the plug of PDMS from the end of the blunt needle before pulling the blunt needle back through the PDMS to leave a port.

Biopsy Punch Technique

Put a piece of scrap PDMS flat on your bench and use a biopsy punch to push through the PDMS. Be very careful to punch strain down and please don’t bend the tip of the biopsy punch (this renders them basically useless). Eject the plug of PDMS before pulling the biopsy punch back through the PDMS to leave a hole.

- The red, 1.20 micrometer diameter biopsy punch works well for making holes that 24AWG tubing can fit snuggly into.

Plasma bonding the PDMS chip to the coverslip

1. Go to the communal lab on the second floor, 2005 of the engineering centers building. Bring scotch tape, 12-544-G 22X60-1.5 microscope cover glass, and your PDMS chip(s) with you.
2. Clean the channel side of the chip using scotch tape. Press and remove scotch tape 3X’s from the channel side of the chip.
3. Open the glass door of the plasma chamber and remove the long flat layer of glass inside.
4. Place your chip (tape free) and a microscope cover glass on the layer of glass. Make sure that the PDMS chip is channel-side up. The sides of the PDMS and glass which are exposed to the air are the parts that will stick to each other. File:Bhattacharya2005.pdf explains the chemistry.
5. Put the layer of glass with your PDMS chip and coverslip back into the plasma chamber. Close the door tightly (may require a strong squeeze!).
6. Press the red power switch, then press the green "Pump" button (it should light up, if it does not light up, the glass door is not closed tightly enough). If the vacuum pump does not immediately turn ON too, turn it ON
7. Send oxygen from the tank on your right to the plasma chamber
8. On the Plasma Chamber, press the yellow "Gas" button to let air flow from the oxygen tank to the chamber.
9. Adjust the black knob until the small black floating ball hovers near 7 in the vertical tube (where my finger is pointing).
10. Wait about 20 seconds for the vacuum to suck out air and for the oxygen to fill the chamber.
11. Use the double arrows to set the pump to stay on for 0.2 minutes (12 seconds). Press the "Generator" button. You should see a whitish-purple plasma.
12. After it has finished, turn off the "Gas" and the "Pump". Turn on the "Ventilation", then pull the door open (may require a good pull).
13. Shut both valves on the oxygen tank.
14. Remove the chip and glass coverslip, and put the PDMS channel-side down on the glass (onto the side of the glass that was facing up). You should see the PDMS bond to the glass.
15. For extra bonding, bake the chip in the oven at 65°C for a few hours or overnight.

Designing PCB via Altium Tutorial 11/04/2019

Jacky Tian - Dec 10, 2019, 12:34 AM CST

Title: Designing PCB via Altium Tutorial

Date: 11/04/2019

Content by: Jacky Tian

Present: Team

Content: Link to the tutorial: https://www.pcbcart.com/article/content/Altium-PCB-design-tutorial.html

This tutorial introduced how to update the PCB from the schematic, how to set up shape and layer, how to mount holes and do routing.

SMD Soldering Updated 12/07/19

Jacky Tian - Dec 09, 2019, 11:02 PM CST

Title: SMD Soldering

Date: 12/07/2019

Content by: Jacky Tian

Present: Jacky Tian & Ruochen Wang

Goals: SMD soldering can be an alternative to hand-solder. Our hand-solder last year was very time-consuming and frustrating. The solders were very easy to break

Content: The LEDs are tiny so it is hard to solder wires to the pins by hands and, since the pins are small, the pins and solder will easily fall apart. Therefore, SMD can be an alternative to hand soldering. We will use SMD paste and hot-air machine which is used to consolidate the paste which is in liquid at first and become solid after being heat.

A useful link to surface mount soldering: https://www.freetronics.com.au/pages/surface-mount-soldering-with-a-toaster-oven#.Xe8kZuhKiUl

Tools and equipment for hot-air soldering:

Hikko Hot-air machine available at Makerspace

- The syringe contains solder paste, which is a mixture of very small solder particles and flux. Pressing on the syringe plunger forces the solder paste through a blunt needle, which is often used to apply solder and flux directly to the PCB pads before placing the surface mount components. Solder paste is also available in small jars, from which the paste may be transferred to a syringe or applied directly to the PCB using a very small tool to dip in the paste and dab on the pads.
- Solder wire is used (with a hand soldering iron) to touch up or clean up joints that are shorted to adjacent pins or joints that are poorly connected.
- Isopropyl alcohol is used along with a soft toothbrush, cotton swabs, and/or a cloth to clean the surface of PCBs before soldering and to remove flux residue after soldering. The alcohol shown is almost 100% pure, but a lesser concentration (such as 91% pure) can also be used if additional time is allowed for the residual water to evaporate.
- Flux is necessary to obtain good flow and coverage of molten solder. In addition to liquid flux (as shown), flux is also available in a pen-style applicator and in gel form for application with a syringe and blunt needle.
- A pair of bent-nose tweezers is useful for handling SMDs; a vacuum pickup tool is another option.
- Solder braid is used (with a hand soldering iron) to remove excess solder from component leads, thereby eliminating shorts between pins. Solder braid is available in different widths for various component sizes; both 2.0mm and 3.0mm (shown) are useful.

Conclusions/action items: Figured out how to use the alternative to solder our wires to the pins on LEDs via SMD soldering and a hot-air machine

Flexible PCB Design 02/16/2020

Jacky Tian - Feb 26, 2020, 3:12 PM CST

Title: Flexible PCB Design

Date: 02/16/2020

Content by: Jacky Tian

Goals: To look for whether there is any PCB available in the market that our team can use

Content: Rigid PCBs typically cost less than flex circuits. Many electronic devices (laptop and desktop computer, flat-screen TVs and monitors, children's toys, and various electronic gadgets) employ rigid PCBs instead of flexible PCBs. However, flex circuits may be found in ultra-compact and/or high-performance devices, including GPS units, tablets, smart phones, cameras, and wearables.

Some links to Flexible PCB that can support our design this semester:

https://www.pcbway.com/Member/Login/?returl=https%3a%2f%2fmember.pcbway.com

https://www.flexiblecircuit.com/product-category/flex-printed/

http://viventi.pratt.duke.edu/ (Viventi Lab at Duke University)

02/13/2020 DC Barrel Jack

Title: Purchase of DC Barrel Jack

Date: 02/13/2020

Content by: Jacky Tian

Goals: Our team needs a DC Barrel Jack to power supply the PCB

Content: https://www.aliexpress.com/item/32818058518.html?src=google&src=google&albch=shopping&acnt=494-037-6276&isdl=y&slnk=&plac=&mtctp=&albbt=Google_7_shopping&aff_platform=google&aff_short_key=UneMJZVf&&albagn=888888&albcp=1582410664&albag=59754279756&trgt=743612850

04/10/2020 Gelatin Research

Jacky Tian - Apr 29, 2020, 12:55 PM CDT

Title: Research on gelatin

Date: 04/10/2020

Content by: Jacky Tian

Goals: Research on gelatin

Content:

Component of gelatin: https://www.peta.org/about-peta/faq/what-is-gelatin-made-of/

Order gelatin online: https://www.amazon.com/Great-Lakes-Unflavored-Gelatin-Kosher/dp/B0008D6WBA?ref_=fsclp_pl_dp_1

Biosafety Training

Jacky Tian - Oct 09, 2019, 2:22 PM CDT

University of Wisconsin-Madison

This certifies that JACKY TIAN has completed training for the following course(s):

Curriculum	Group Name	Completion Date	Expiration Date
Assurance	Stem Cell Ethics and Policy Training	9/12/2018	
Biosafety Required Training Quiz	Biosafety Required Training	3/11/2018	

Data Effective: Thu Sep 13 6:38:59 2018
Report Generated: Mon Sep 17 00:48:06 2018

10/31/2019 Altium documents from BME 462

Lisa Xiong - Nov 01, 2019, 12:23 PM CDT

Title: Document Altium documents from BME 462 Labs for PCB design reference

Date: 10/31/2019

Content by: Lisa

Present: n/a

Goals: To document Altium notes from BME 462. These guides will be useful for future students who need some help to start on Altium if they continue this project.

Content:

Attached to this entry are labs 7 and 8, BME 462 labs where we worked on PCB boards. This is a very rough overview and does not encompass all the tools available in Altium.

Conclusions/action items:

Document some files that could help with understanding how to use and design with Altium.

10/17/2019 Altium Notes (BME 462)

Lisa Xiong - Dec 09, 2019, 2:33 PM CST

Title: Altium Notes

Date: 10/17/2019

Content by: Lisa

Present: n/a

Goals: To document Altium learned in BME 462 to use in our design project

Content:

Goals of Altium today:

- Footprint
- Create a symbol
- Put the symbol onto our schematic

Next goals of Altium lecture:

- How to put parts on board
- How to route parts to create circuit board

Altium Notes:

- Creating a project
    - File>New>Project
- Creating a new schematic
    - Right click the project name>add new to project>schematic
- Creating a symbol (for those not in the library)
    - Right click project name>add new to project>schematic library
    - The toolbox on the top of the screen allows you to add pins and shape of the symbol
    - White dots on the pins allow you to make a connection and make sure that they are secure
        - YOUR WHITE DOTS NEED TO FACE OUTWARDS
    - You can label your pins by right-clicking the pins and changing designator and name
- How to zoom in and out
    - CTRL+SCROLL WHEEL
- How to place newly built component into your schematic
    - Place part>choose library from top drop down menu>double click the component you want
- Creating your footprint
    - Right-click your project>add new to project>PCB library

Conclusions/action items:

These are some notes that I took in class that might be helpful for when we design our own PCB.

12/9/2019 First PCB Design

Lisa Xiong - Dec 10, 2019, 9:50 AM CST

Title: First PCB Design

Date: 12-9-2019

Content by: Lisa

Present: none

Goals: To document the first PCB design I created on Altium and discuss why this was a bad design.

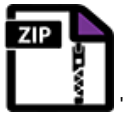
Content:

- After consulting with the team we determined that we wanted 4 LEDs powered in parallel
  - This was also confirmed with Amit
- The PCBs are connected in series in terms of the Din and Dout pins. LED #1 (top right LED) is connected to the microcontroller. The Dout pin of LED #1 connects to Din of LED #2 and so on. This allows the same signal from the microcontroller to be sent to the rest of the LEDs to do the same thing.
- Although the concept was good, this design was bad because it utilized through hole footprints. This was my first time developing an SMD PCB, so once we realized this was an issue we redeveloped a brand new PCB to reflect this change.

Conclusions/action items:

We have a very "pretty" design but was non-functional because the SMD pads would not be able to connect to the PCB. Changes had to be made to the design to allow SMD soldering for the LEDs.

Lisa Xiong - Dec 09, 2019, 2:40 PM CST



BME400_480nmLED.zip(17.7 MB) - download This is a zip file of the first PCB design our team came up with. The zip file contains the PCB project, schematic file, PCB file, PCB library and schematic library.

12/9/2019 Second PCB Design

Lisa Xiong - Dec 10, 2019, 9:53 AM CST

Title: Second PCB Design

Date: 12/9/2019

Content by: Lisa Xiong

Present: n/a

Goals: To document an alternative PCB design utilizing a "jut" that would stick out of the mouse and away from the main PCB to reduce risk of electrocution.

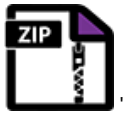
Content:

- There were no significant differences in this design compared to design #1. The LEDs were connected all in the same way, and the three through holes were connected at a farther location on the PCB.
- The PCBs are connected in series in terms of the Din and Dout pins. LED #1 (top right LED) is connected to the microcontroller. The Dout pin of LED #1 connects to Din of LED #2 and so on. This allows the same signal from the microcontroller to be sent to the rest of the LEDs to do the same thing.
- Although the concept was good, this design was bad because it utilized through hole footprints. This was my first time developing an SMD PCB, so once we realized this was an issue we redeveloped a brand new PCB to reflect this change.

Conclusions/action items:

Hanna suggested this as a potential design. Our team really liked the three through hole ideas and moved forward with that but not the jutted portion since it would increase PCB size. We have a very "pretty" design but was non-functional because the SMD pads would not be able to connect to the PCB. Changes had to be made to the design to allow SMD soldering for the LEDs.

Lisa Xiong - Dec 09, 2019, 3:23 PM CST



PCB-Project_JUT.zip(4.5 MB) - download This is a zip file of the second proposed PCB design our team came up with. The zip file contains the PCB project, schematic file, PCB file, PCB library and schematic library. What makes this different from the first iteration is that it has thru holes that "jut" away from our LEDs. We hope that this could potentially stick out of the mouse to reduce potential electric shock.

2/26/2020 PCB Design for the 480 nm LEDs

Lisa Xiong - Feb 26, 2020, 10:41 AM CST

Title: PCB Design for the 480 nm LEDs

Date: 2/26/2020

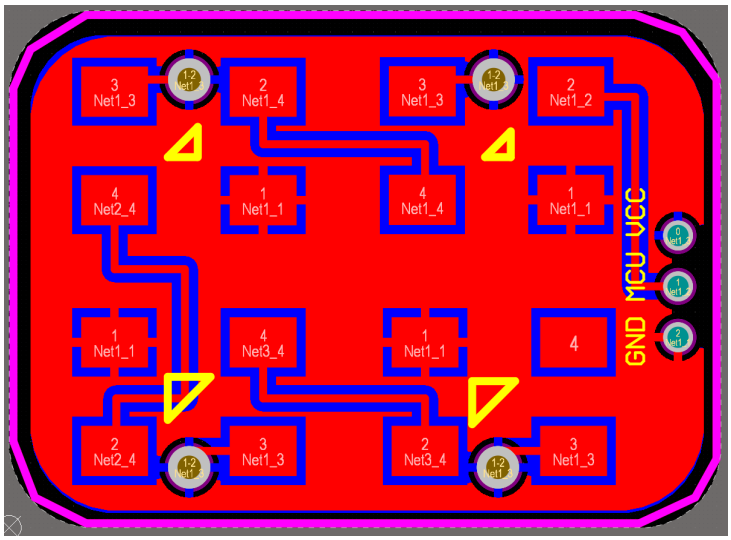
Content by: Lisa Xiong

Present: n/a

Goals: To document the new PCB for the 480 nm LEDs

Content:

The new PCB features larger SMD pads since that was the largest factor that prevented us from being able to solder effectively. Instead of having two polygon pours, we will have one polygon pour that will be connected to ground and the MCU and VCC connections will be connected via traces on the top layer. This will simplify our design so that it will be compatible for prototype printing at the MakerSpace.



Conclusions/action items:

Document the PCB designed for the 480 nm LEDs.

9/12/2019 Background on Client and Current Research

Lisa Xiong - Sep 13, 2019, 3:35 PM CDT

Title: Background on Client

Date: 9/12/2019

Content by: Lisa

Present: n/a

Goals: To learn about our client's background and his research goals.

Content:

Focus of study:

- Studies role of T cells in granulomatous immune responses
    - Looking at infection agents including Schistosoma mansoni, Leishmania donovani, and Mycobaterium bovis
- Uses animal models to understand how granulomas protect the host, but also cause diseases
- Understand how T-cells fight chronic infections
- Understand how T-cells work together
- Understand how antibodies and antibody associated pathways interfere with T-cell responses

Overall goal:

- Create more effective vaccines and better treatments for granulomatous diseases

Conclusions/action items:

Dr. Sandor is focused on understanding t-cells and their immune responses. He is particularly interested in how they cause diseases in the human body. By understanding t-cells and their influences in the human body, he hopes to develop improved and more effective vaccines for granulomatous diseases.

9/13/2019 A toolbox of Cre-dependent optogenetic transgenic mice for light-induced activation and silencing

Lisa Xiong - Sep 13, 2019, 3:41 PM CDT

Title: A toolbox of Cre-dependent optogenetic transgenic mice for light-induced activation and silencing

Date: 9/13/2019

Content by: Lisa

Present: n/a

Goals: To understand how Professor Sandor uses cell light sensitivity to observe

Content:

Conclusions/action items:

9/15/2019 A Compact Parylene-Coated WLAN FlexibleAntenna for Implantable Electronics

Lisa Xiong - Sep 15, 2019, 2:37 PM CDT

Title: A compact parylene-coated WLAN flexible antenna for implantable electronics

Date: 9/15/2019

Content by: Lisa

Present: n/a

Goals: To learn about how parylene was used for an implantable electronic device

Content:

- There is an increased use of bio-compatible and bio-integrated flexible electronics for research
- Current approaches limit a fully-implantable system, as a result of the electronics not being able to communicate wirelessly or device powering limitations
- Wireless antennas operating in a wireless local area network (WLAN) can provide high-speed transmission pathway that can be combined with other devices
- An antenna was created and coated with an 10micrometer thick parylene-C using chemical vapor deposition process
    - Parylene-C has the ability to minimize oxygen contamination
- Parylene-C coating had negligible effect on the antenna performance

Conclusions/action items:

Y.H. Jung, Y. Qiu, S. Lee, T.Y. Shih, Y. Xu, R. Xu, J. Lee, A. Schendel, W. Lin, J.C. Williams, N. Behdad, Z. Ma, "A Compant Parylene-Coated WLAN Flexible Antenna for Implantable Electronics," IEEE ANTENNAS AND WIRELESS PROPAGATION LETTERS, vol. 16, 2016. [Online]. Available: https://ieeexplore.ieee.org/stamp/stamp.jsp?arnumber=7360913. [Accessed Sep. 15, 2019]

9/15/2019 Materials and designs for wirelessly powered implantable light-emitting systems

Lisa Xiong - Sep 15, 2019, 5:34 PM CDT

Title: Materials and designs for wirelessly powered implantable light-emitting system

Date: 9/15/2019

Content by: Lisa

Present: n/a

Goals: To learn about how other light-emitting systems were implanted - this will help me learn what methods we could explore now that we have already completed the specifications for the light intensity and wavelengths.

Content:

- The journal is a presentation of different strategies to implant light emitting diodes with wireless scheme
- Electronic components are transferred onto PDMS and stamped onto a flexible substrate
    - These devices are different than our project since they are creating the semi-conductor and LED on the flexible substrate
    - Our device is different due to using a pre-fabricated micro LED
- These designs have a lot of applications for disease/theraputic treatment
- PET substrate encapsulated by PDMS did not cause any inflammatory reactions in the tissues

Conclusions/action items:

PDMS is a good start to what we could use the encapsulate our device in-however we still have to figure out related issues in terms of the heatsink. This model was very thin and had a large surface area, and did not require a wire to operate...

Kim, R., Tao, H., Kim, T., Zhang, Y., Kim, S., Panilaitis, B., Yang, M., Kim, D., Jung, Y., Kim, B., Li, Y., Huang, Y., Omenetto, F. and Rogers, J. (2012). *Materials and Designs for Wirelessly Powered Implantable Light-Emitting Systems*. [Online] Wiley Online Library. Available at: https://onlinelibrary.wiley.com/doi/full/10.1002/smll.201200943 [Accessed 15 Sep. 2019].

9/15/19 Heatsink

Lisa Xiong - Sep 15, 2019, 5:50 PM CDT

Title: Heat sink

Date: 9/15/2019

Content by: Lisa

Present: n/a

Goals: To learn what a heat sink is

Content:

- A heat sink is a passive heat exchanger that transfers heat generated by an electronic/mechanical device to a different medium which is therefore dissipated.
- Heat sinks regulate temperature, keep systems cool, and prevent overheating
- Often used with LEDs where heat dissipation via the device itself is not sufficient
- Designed to maximize its surface area, increased surface area means more space to release energy to
- Usually made out of copper or aluminum since they are generally good conductors

Conclusions/action items:

Heat sinks are very important in regulating the temperature for the LEDs we will be using. However, we will not be able to use a metal heatsink since it may react in the mouse's body, also we are unsure if it is bio compatible. We will need to do more research on bio-compatible heat sinks.

"Heat sink" in Wikipedia: the Free Encyclopedia [Online], Sep. 15, 2019. Available: https://en.wikipedia.org/wiki/Heat_sink. [Sep. 15, 2019]

9/16/2019 Pulse Wave (PM) Modulation

Lisa Xiong - Oct 08, 2019, 9:38 PM CDT

Title: Pulse wave modulation

Date: 9/16/2019

Content by: Lisa

Present: n/a

Goals: To learn about pulse wave modulation

Content:

- Pulse wave modulation (PWM) is a type of digital signal
- Common use is to dim RGB leds or control a motor
- PWM allows us to vary how much time the signal is high analog wise
    - The "high" value depends on the microcontroller, for arduino usually 3.3V or 5V
- Duty cycle - the percentage of time a signal is "high"
- The higher the frequency, the less obvious it is that a signal is going from high to low
- The main idea is that PWM can be used for control - by controlling the power of a device using PWM, there are many applications depending on what you want to use it for
    - For our project, consider PWM for the channels in mouse brain

Conclusions/action items:

PWM is the idea of setting the output of a signal at high or low. This simple "on" and "off" control has many uses and applications, depending on what you are trying to achieve.

9/16/2019 Fundamentals for bioheat transfer

Lisa Xiong - Oct 08, 2019, 9:49 PM CDT

Title: Fundamentals for bioheat transfer

Date: 10/8/2019

Content by: Lisa

Present: n/a

Goals: Understand how heat is transferred in biology

Content:

- Heat transfer is the energy flow created by the difference in temperature between two points
- Always flow from hot to cold
- Three main types of energy:
    - Stored energy - potentials like thermal, chemical, kinetic, electric, and magnetic
    - Heat transfer - temperature level differences between two systems
    - Work - Energy in transition due to forces acting between systems
- First law is important for thermodynamics - THE CONSERVATION OF ENERGYYYY
    - Energy cannot be created or destroyed, can only be transformed
- To access the rest of the document you have to pay a fee...

Conclusions/action items:

There are multiple methods of energy transfer. This source was very basic and did not go in-depth to tissue bioheat related energy because there was a paywall. Very unfortunate.

Reference: Chato J.C. (1990) Fundamentals of Bioheat Transfer. In: Gautherie M. (eds) Thermal Dosimetry and Treatment Planning. Clinical Thermology (Subseries Thermotherapy). Springer, Berlin, Heidelberg

https://link.springer.com/chapter/10.1007/978-3-642-48712-5_1

9/16/2019 Parylene C how it is applied

Lisa Xiong - Oct 08, 2019, 9:58 PM CDT

Title: Parylene C - How it is applied

Date: 10/8/2019

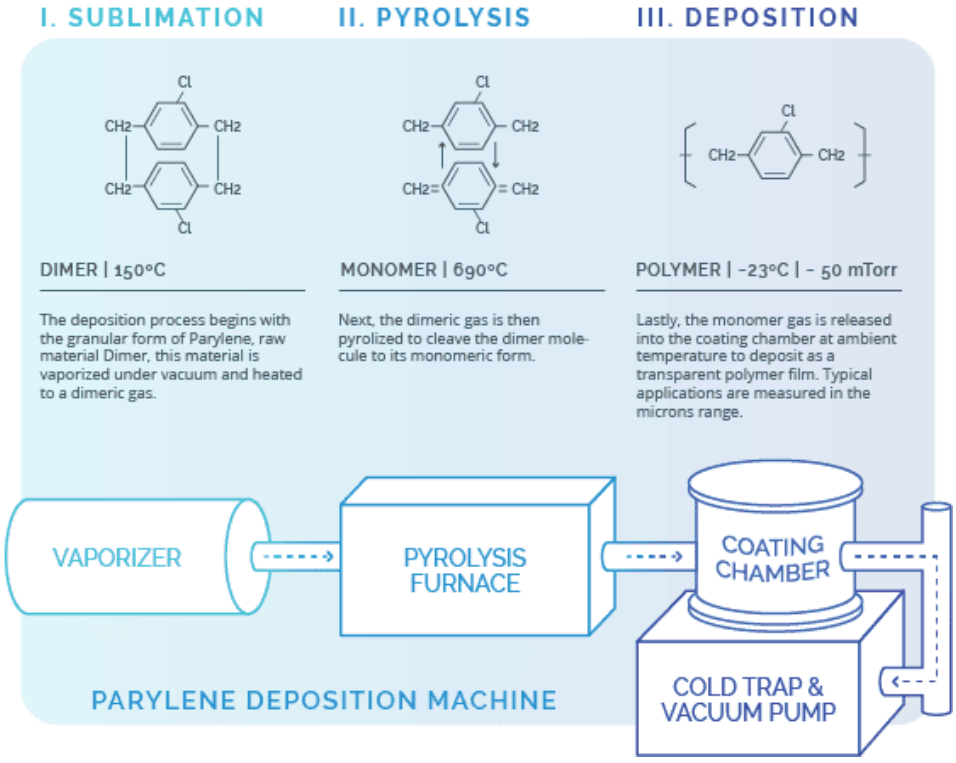
Content by: Lisa

Present: n/a

Goals: To learn how Parylene C is applied to electronics.

Content:

- Parylene is coated by a method called Chemical Vapor Deposition
- Parylene films are grown in a vacuum chamber at room temperature
    - Result is pin-hole free coating without byproducts
- Thin film is very uniform
- Before application, parts usually undergo a "primer" step
    - This helps parylene attach onto electronics
- Parylene-C is the most popular substrate because of its strong barrier and dielectric properties
    - Best for: implants, pin-hole free barrier layers, and encapsulating electrical components



Conclusions/action items:

Parylene-C is applied onto microelectronics via a vapor deposition. Because of this vapor application, it allows for a THIN film and pin-hole free coating that makes it good use for implants.

Reference: vsiparylene, *The Parylene Deposition Process*, Broomfield, CO, United States, 2019. Accessed on: 8-10-2019. [Online]. Available: https://vsiparylene.com/parylene-advantages/process/

10/8/2019 Advances in Materials for Recent Low-Profile Implantable Bioelectronics

Lisa Xiong - Oct 08, 2019, 10:10 PM CDT

Title: Advances in Materials for Recent Low-Profile Implantable Bioelectronics

Date: 10/8/2019

Content by: Lisa

Present: n/a

Goals: To understand what products are used out in the market to coat electronics for implantable purposes.

Content:

- This paper documents 6 organic materials that are used for biocompatible implants
    - PDMS: Low modulus, high dielectric strength, low chemical reactivity
    - Medical grade silicone: High tear strength and elasticity, transperancy
    - Parylene-C: chemically and biologically inert, low water permeability and absorption
    - Polyimide: High heat resistance
    - PVDF(Polyvinylidine fluoride): Pizoelectricity
    - LCP(Liquid crystal polymer): Low dielectric constant and low moisture absorption rate
- The three materials of interest are PDMS, medical grade silicone, and parylene-c

Conclusions/action items:

There are more biocompatible materials out there than I thought - paryleneC is probably still our best interest because of its wide use in the literature and proven functionality for implants.

Y. Chen, Y-S. Kim, B. Tillman, W-H. Yeo, Y. Chun, "*Advances in Materials for Recent Low-Profile Implantable Bioelectronics*," Materials (Basel), 11(4), pp. 522, April, 2018. [Online] Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5951368/

12/10/2019 Flexible, stretchable and implantable PDMS encapsulated cable for implantable medical device

Lisa Xiong - Dec 10, 2019, 10:35 AM CST

Title: Flexible, stretchable and implantable PDMS encapsulated cable for implantable medical device

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document a prototype that used PDMS to encapsulate and implant a cable for a medical device.

Content:

- Kim et. al developed a biocompatible, flexible, and durable cable encapsulated by PDMS to be used to connect medical devices in the body for transcutaneous energy or signal transfer.
- They were able to develop a mechanically stable and biocompatible cable suitable for long term implantable medical devices.

Conclusions/action items:

PDMS has been successfully used in an implantable cable designed to connect medical devices in the human body.

Reference: Kim, S.H., Moon, JH., Kim, J.H. et al. Biomed. Eng. Lett. (2011) 1: 199. https://doi.org/10.1007/s13534-011-0033-8

12/10/2019 USHIO SP500 and SP250 spot UV curing equipment

Lisa Xiong - Dec 10, 2019, 10:28 AM CST

Title: USHIO SP500 and SP250 spot UV curing equipment

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document a light source used to photoconvert KikGR33 mouse cells in previous research papers.

Content:

Tomura et. al utilized an USHIO SP500 to photoconvert their KikGR33 mouse cells. Tomura is an author for several other KikGR research papers and has also utilized the SP250 model [1][2]. This device uses a UV lamp as the light source instead of a fiber optic cable or LED.

Figure 1: *An image of the USHIO Spot-Cure Series, Spot UV Curing Equipment [3].*

Conclusions/action items:

This device has been used for KikGR33 photoconversion. USHIO manufactures many other devices and does sell LEDs (however not in the 405nm range).

[1] M. Tomura, A. Hata, S. Matsuoka, F. H. W. Shand, Y. Nakanishi, R. Ikebuchi, S. Ueha, H. Tsutsui, K. Inaba, K. Matsushima, A. Miyawaki, K. Kabashima, T. Watanabe, O. Kanagawa, "Tracking and quantification of dendritic cell migration and antigen trafficking between the skin and lymph node," Scientific Reports, vol. 4, no. 6030, Aug. 2014. [Online] Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4129424/

[2] M. Tomura, T. Honda, K. Tanizaki, A. Otsuka, G. Egawa, Y. Tokura, H. Waldmann, S. Hori, J. G. Cyster, T. Watanabe, Y. Miyachi, O. Kanagawa, K. Kabashima, "Activated regulatory T cells are the major T cell type emigrating from the skin during a cutaneous immune response in mice, " The Journal of Clinical Investigation, vol. 120, no. 3, pp. 883-893. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2827959/

[3] USHIO, Deep UV Lamp Spot-Cure Series - Spot UV Curing Equipment, Tokyo Instruments, 2019. Accessed on: December. 9, 2019. [Online]. Available: http://www.tokyoinst.co.jp/en/products/detail/UD02/index.html

12/10/2019 Leica Microsystems fluorescence stero microscope

Lisa Xiong - Dec 10, 2019, 10:28 AM CST

Title: Blue Sky Research's FiberTec II™ Series

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document another device used to photoconvert KikGR33 mouse cells. This is a different manufacturer from USHIO (Japan based company).

Content:

Tomura et. al used a Leica Microsystems fluorescence stereo microscope to photoconvert KikGR33 mouse cells [1].

Figure 1: *Leica M205 FA fluorescence microscope [2]. This is not the same one used in the paper, just a representation of what one of their stereo microscopes look like.*

Conclusions/action items:

The Leica Microsystems fluorescence stereo microscope is another competing design.

[1] M. Tomura, N. Yoshida, J. Tanaka, S. Karasawa, Y. Miwa, A. Miyawaki, O. Kanagawa, "Monitoring cellular movement in vivo with photoconvertible fluorescence protein "Kaede" transgenic mice," Proceedings of the National Academy of Sciences of the United States of America, vol. 105, no. 31, pp. 10871-10876. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2504797/

[2] Leica Microsystems, "Fluorescence stereo microscopes Leica M205 FCA & Leica M205 FA," Leica Microsystems. 2019. [Online]. Available at: https://www.leica-microsystems.com/products/stereo-microscopes-macroscopes/p/leica-m205-fca/. [Accessed 12/10/2019].

12/10/2019 Blue Sky Research’s FiberTec II™ Series

Lisa Xiong - Dec 10, 2019, 10:30 AM CST

Title: Blue Sky Research’s FiberTec II™ Series

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document a device used in the scientific literature to photoactivate Ai32 mouse cells.

Content:

Prabhakar et. al used a Fibertec II Fiber Coupled Diode Laser Module (Blue Sky Research) to photoactivate Ai32 mouse cells [1].

Figure 1: *Blue Sky Research’s FiberTec II™ Series uses fiber-coupled lasers that incorporate modulation and feedback functions [2].*

Conclusions/action items:

Blue Sky Research is a company that manufactures microscopes, light sources, etc. for imaging research.

[1] A. Prabhakar, D. Vujovic, L. Cui, W. Olson, W. Luo, B. Arenkiel, "Leaky expression of channelrhodopsin-2 (ChR2) in Ai32 mouse lines," PLOS One, vol. 14, no. 3. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6435231/

[2] Blue Sky Research, Fiber Coupled Lasers, Blue Sky Research, 2019. Accessed on: December. 9, 2019. [Online]. Available: https://blueskyresearch.com/products/fiber-coupled-lasers-and-systems/fiber-coupled-lasers/

9/15/19 Parylene

Lisa Xiong - Dec 10, 2019, 10:56 AM CST

Title: Parylene

Date: 9/15/19

Content by: Lisa

Present: n/a

Goals: To learn what Parylene is and how we can potentially use it in our project

Content:

- Parylene is a polymer used as a moisture and dielectric barrier
- Parylene is another alternative to PDMS that could be used as a protective coating
- Characteristics and advantages
    - Hydrophobic
    - Good barrier properties for inorganic and organic media, strong acids, caustic solutions, gases and water vapor
    - Low dielectric constant
    - Biostable and biocompatible
    - Corrosive resistant
    - Homogeneous surface
    - Moisture absorption less than 0.1% after 24 hours
- Gold standard for encapsulation of implantable devices

Conclusions/action items:

"Parylene" in Wikipedia: the Free Encyclopedia [Online], Sep. 15, 2019. Available: https://en.wikipedia.org/wiki/Parylene. [Sep. 15, 2019]

S. Hornm "Silicone Conformal Coating vs. Parylene," Diamond-MT, Conformal Coating, August. 7, 2015. [Online]. Available: https://blog.paryleneconformalcoating.com/silicone-conformal-coating-vs-parylene. [Accessed: December 9, 2019].

12/10/2019 MIT, properties of PDMS

Lisa Xiong - Dec 10, 2019, 10:43 AM CST

Title: MIT, properties of PDMS

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To learn about PDMS properties.

Content:

Table 1: PDMS properties

Property	Value	Reference	Image/URL (optional)
Mass density	0.97 kg/m^3	Polymer Data Handbook, Mark J., Oxford Univ. Press, New York (1999)	
Young's modulus	360-870 KPa	Re-configurable Fluid Circuits by PDMS Elastomer Micromachining	http://mass.micro.uiuc.edu/publications/papers/26.pdf
Poisson ratio	0.5	Polymer Data Handbook	
Stiffness Constants			
Tensile or fracture strength	2.24 MPa	Polymer Data Handbook	
Residual stress on silicon			
Specific heat	1.46 kJ/kg K	Polymer Data Handbook	
Thermal conductivity	0.15 W/m K	Polymer Data Handbook	
Dielectric constant	2.3-2.8	Polymer Data Handbook	
Index of refraction	1.4	Polymer Data Handbook	
Electrical conductivity	4x10^{13} Ωm	Polymer Data Handbook	

Magnetic permeability	$0.6x10^6$ cm^3/g	Polymer Data Handbook	
Piezoresistivity	N/A		
Piezoelectricity	N/A		
Wet etching method	tetrabutylammonium fluoride ($C_{16}H_{36}FN$) + n-methyl-2-pyrrolidinone (C_5H_9NO) 3:1	J. Garra, T. Long, J. Currie, T. Schneider, R. White, M. Paranjape, “Dry Etching of Polydimethylsiloxane for Microfluidic Systems”, Journal of	http://scitation.aip.org/journals/doc/JVTAD6-ft/vol_20/iss_3/975_1.html
Plasma etching method	CF_4+O_2	J. Garra, T. Long, J. Currie, T. Schneider, R. White, M. Paranjape, “Dry Etching of Polydimethylsiloxane for Microfluidic Systems”, Journal of Vacuum Science and Technology, A20, pp 975-982, 2002.	http://scitation.aip.org/journals/doc/JVTAD6-ft/vol_20/iss_3/975_1.html
Adhesion to silicon dioxide	Excellent	Re-configurable Fluid Circuits by PDMS Elastomer Micromachining	http://mass.micro.uiuc.edu/publications/papers/26.pdf
Biocompatibility	Noniritating to skin, no adverse effect on rabbits and mice, only mild inflammatory reaction when implanted	Polymer Data Handbook; Belanger MC, Marois Y. Hemocompatibility, biocompatibility, inflammatory and in vivo studies of primary reference materials low-density polyethylene and polydimethylsiloxane: a review. J Biomed Mater Res 2001;58(5):467–77.	
Hydrophobicity	Highly hydrophobic, contact angle 90-120°	Re-configurable Fluid Circuits by PDMS Elastomer Micromachining	http://mass.micro.uiuc.edu/publications/papers/26.pdf

Melting Point	-49.9–40°	Knovel Critical Tables	

Conclusions/action items:

Massachusetts Institute of Technology published a table of properties of PDMS.

Massachusetts Institute of Technology, "Material: PDMS (polydimethylsiloxane)," Massachusetts Institute of Technology. [Online]. Available: http://www.mit.edu/~6.777/matprops/pdms.htm. [Accessed: December 10, 2019].

12/10/2019 UV SMD LED PLCC-2

Lisa Xiong - Dec 10, 2019, 10:43 AM CST

Title: UV SMD LED PLCC-2

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document the 405 nm LED datasheet.

Content:

The 405 nm LED is a two pin device that has a fixed wavelength but varied brightness depending on the voltage input. The voltage input range is 0-5V.

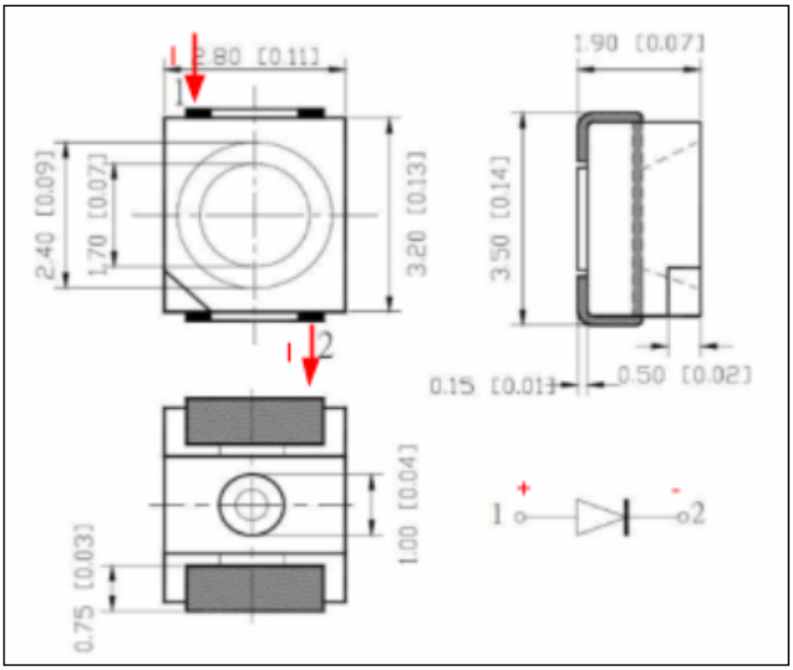


Figure 1: *The LED for the 405nm wavelength is a two pin diode. Current will flow into pin 1 and out of pin 2, continuing onto the next LED.*

Conclusions/action items:

The 405 nm LED is a very simple and easy to use device.

Vishay Semiconductors, “UV SMD LED PLCC-2,” VLMU3100 datasheet, 26-June-2017. Accessed on: 8-Oct-2019.

12/10/2019 SK6812 SPECIFICATION INTEGRATED LIGHT SOURCE INTELLIGENT CONTROL OF CHIP-ON-TOP SMD TYPE LED

Lisa Xiong - Dec 10, 2019, 10:47 AM CST

Title: SK6812 SPECIFICATION INTEGRATED LIGHT SOURCE INTELLIGENT CONTROL OF CHIP-ON-TOP SMD TYPE LED

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document the 480 nm LED datasheet.

Content:

The 480 nm LED is a 4 pin RGB pixel LED containing a smart circuit. This allows the LED to communicate with a microcontroller to output specific wavelengths and brightness. The LED has four pins and requires a 5V power input, a ground connection, has a digital input pin to communicate to the microcontroller, and output pin that can send the same microcontroller command to other 480 nm LEDs.

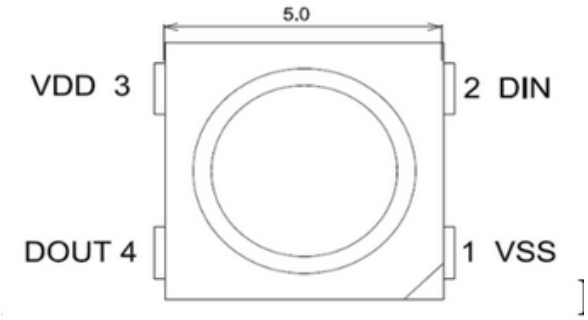


Figure 1: *The 480 nm LED is a 4 pin device. Pin 1 (VSS) is the ground pin, pin 2 (DIN) is the digital input pin that communicates with the microcontroller, pin 3 (VDD) is the power pin where +5 V is input, and pin 4 (DOUT) is the digital output pin where the LED can send the signal it receives from the microcontroller to other LEDs.*

Conclusions/action items:

The 480 nm LED has advantages for its customization ability.

Szledcolor, “SK6812 SPECIFICATION INTEGRATED LIGHT SOURCE INTELLIGENT CONTROL OF CHIP-ON-TOP SMD TYPE LED,” SK6812 Datasheet, 25-April-2016. Accessed on: 8-Oct-2019.

12/10/2019 5050 LED breakout PCB

Lisa Xiong - Dec 10, 2019, 10:55 AM CST

Title: 5050 LED breakout PCB

Date: 12/10/2019

Content by: Lisa

Present: n/a

Goals: To document the break out boards we purchased to prototype with.

Content:

A manufactured breakout board with SMD footprints was ordered to solder the LEDs onto it along with header pins to connect to a breadboard. This PCB is purchasable from Adafruit and is manufactured to be compatible with these 5050 LEDs (480 nm).

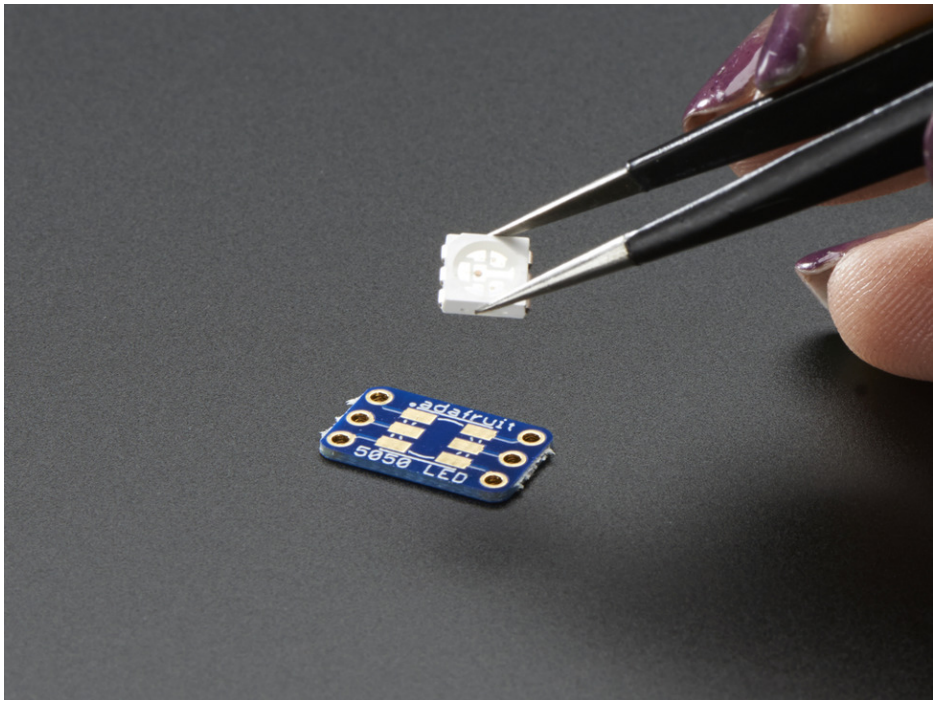


Figure 1: *5050 LED breakout PCB. There are 5050 leds that are 6 pin, ours are four pin and only required the four outermost header pins on the breakout board.*

Conclusions/action items:

The breakout boards are really useful for prototyping, debugging, and making sure our connections are correct.

Adafruit. (2019, December. 9). 5050 LED breakout PCB - 10 pack! [Online]. Available: https://www.adafruit.com/product/1762

9/13/2019 Green Permit

Lisa Xiong - Sep 13, 2019, 2:59 PM CDT

Title: Green Permit

Date: 9/13/2019

Content by: Lisa

Present: Lisa

Goals: To show proof that I obtained my green pass.

Content:

Conclusions/action items:

Lisa Xiong successfully completed her Green Permit training.

9/13/2019 Biosafety Training

Lisa Xiong - Sep 13, 2019, 2:59 PM CDT

Title: Biosafety Training Certification

Date: 9/13/2019

Content by: Lisa

Present: Lisa

Goals: To show proof that I complete the biosafety training.

Content:

Attached to this entry is the pdf that shows I completed the biosafety training.

Conclusions/action items:

Lisa Xiong completed the required biosafety training.

Lisa Xiong - Mar 14, 2018, 12:58 AM CDT


Quiz Submissions - Biosafety Required Training Quiz

Lisa Xiong (username: pxiong55)

Attempt 1

Submission View

Quiz_Submissions_-_Biosafety_Required_Training_Quiz_-_Biosafety_Required_Training_-_Madison_1_.pdf(126.3 KB) - download

9/13/2019 HIPPA Training

Lisa Xiong - Sep 13, 2019, 2:58 PM CDT

Title: HIPPA Training

Date: 9/13/2019

Content by: Lisa

Present: n/a

Goals: To document HIPPA training and certification

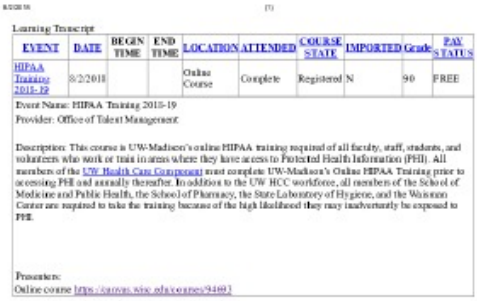
Content:

The attached document is a pdf of my HIPPA certification

Conclusions/action items:

Lisa Xiong is HIPPA certified for the year of 2018 - 2019

Lisa Xiong - Oct 10, 2018, 9:14 AM CDT



Learning Transcript

EVENT	DATE	BEGIN TIME	END TIME	LOCATION	ATTENDED	COURSE STATE	IMPORTED	Grade	PAY STATUS
HIPAA Training 2018-19	8/2/2018			Online Course	Complete	Registered	N	90	FREE

Event Name: HIPAA Training 2018-19

Provider: Office of Talent Management

Description: This course is UW-Madison's online HIPAA training required of all faculty, staff, students, and volunteers who work or train in areas where they have access to Protected Health Information (PHI). All members of the UW Health Care Component must complete UW-Madison's Online HIPAA Training prior to accessing PHI and annually thereafter. In addition to the UW HCC workforce, all members of the School of Medicine and Public Health, the School of Pharmacy, the State Laboratory of Hygiene, and the Waisman Center are required to take the training because of the high likelihood they may inadvertently be exposed to PHI.

Presenters:

Online course https://canvas.wisc.edu/courses/94483

HIPPA_2018.pdf(108 KB) - download

9/13/2019 CITI Training

Lisa Xiong - Sep 13, 2019, 2:58 PM CDT

Title: CITI Training

Date: 9/13/2019

Content by: Lisa

Present: n/a

Goals: To document CITI or Human Subjects Research certification

Content:

Attached is a pdf file of my CITI certificate

Conclusions/action items:

Lisa Xiong has a Human Subjects Research certification

Lisa Xiong - Oct 10, 2018, 9:15 AM CDT

CITI_2018_training.pdf(410.6 KB) - download

4/27/2020 HIPAA Training Certificate

Lisa Xiong - Apr 27, 2020, 10:54 PM CDT

Title: 2020-2021 HIPAA Training Certificate

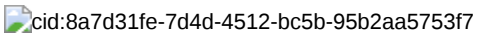
Date: 4/27/2020

Content by: Lisa

Present: n/a

Goals: To document up-to-date certification for HIPAA training.

Content:



Conclusions/action items:

I have HIPAA training and certification for 2020.

Flexible PCB

Ruochen Wang - Feb 26, 2020, 2:21 PM CST

Title: Flexible PCB

Date: 2/10/2020

Content by: Ruochen

Present: Ruochen

Flexible printed circuit boards offer a number of potential benefits including:
• **Saving Space**. Flex PCB design requires only about 10 percent of the space and weight of an ordinary circuit board assembly, offering greater installation and packaging freedom. The inherent flexibility also permits tighter bend capabilities.
• **Maximum Reliability**. A flexible printed circuit board requires fewer interconnects, which in turn requires fewer contact crimps, connectors, and solder joints. Simply put, a flexible PCB board does not contain as many potential sources for failure, which enhances their reliability.
• **Enhanced Capabilities**. The flexible printed circuits boards are compatible with virtually any type of connector or component and work well with options such as ZIP connectors. They also perform extremely well in extreme temperatures and offer superior resistance to radiation and chemicals.
• **Cost Savings**. Cost-saving advantages of Flexible PCBs include reduced material and packaging demands, lower parts replacement costs and assembly errors that could result in the need for repairs.

These benefits make flex PCBs ideally fit for a wide range of applications in industries such as Military, Transportation, Medical, Consumer Electronics, Automotive, Aerospace, Communications, and Industrial.

Altium Design

Ruochen Wang - Feb 26, 2

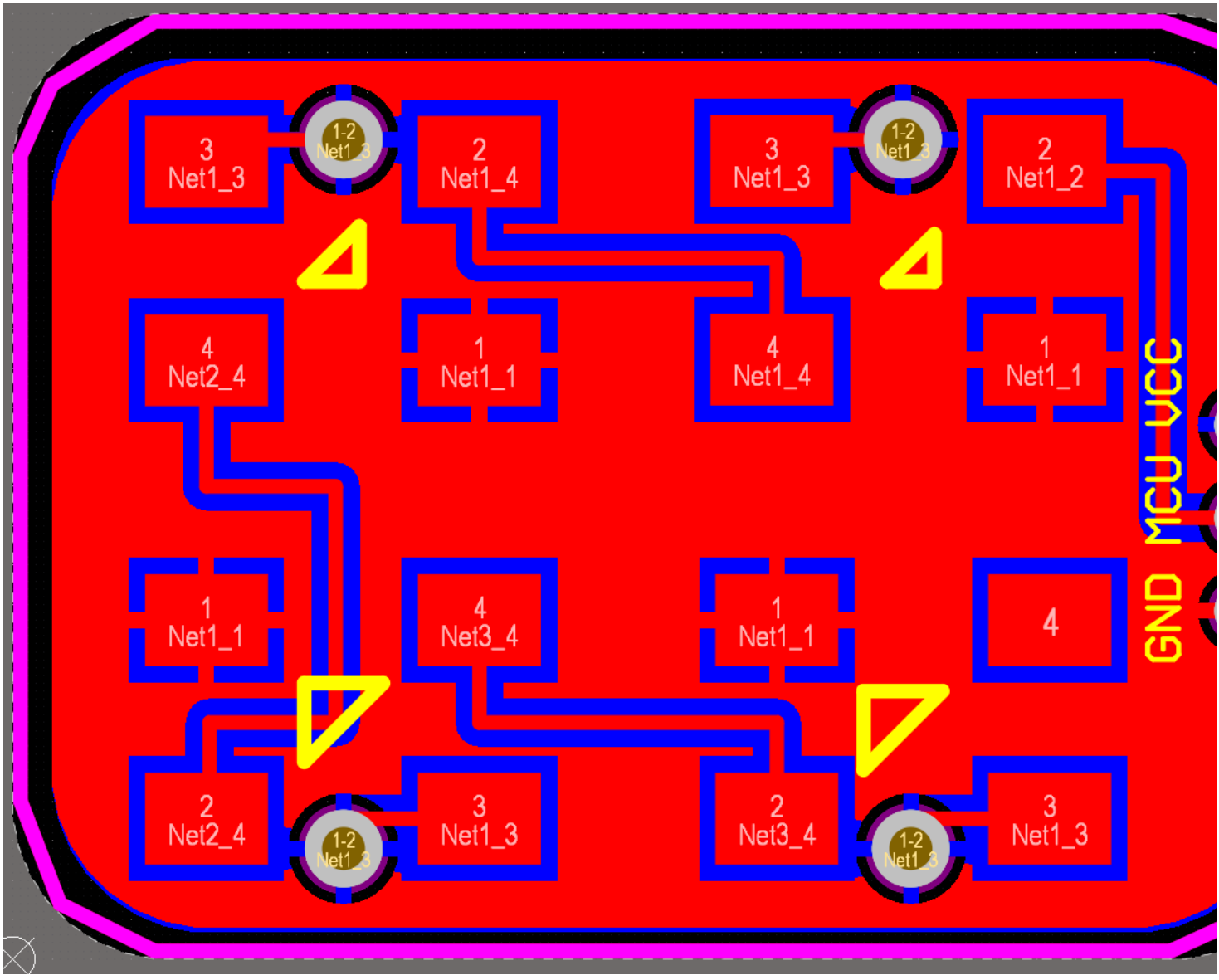
Title: Flexible PCB

Date: 2/15/2020

Content by: Lisa, Ruochen

Present: Ruochen

There are 4 pins on the LEDs, and the data output pin has to connect to the data input pin of the next LED. To fulfill this requirement, vias were used to bypass different wires to avoid crossing image shows the top layer, while the bottom layer is connecting to the VCC and the polygon pour techniques enable every pin of the pad that LEDs will be soldered on connected to the corres



gelatin fabrication

Ruochen Wang - Apr 29, 2020, 2:00 PM CDT

Title: Gelatin Fabrication

Date: 4/15/2020

Content by: Ruochen

Present: Ruochen

A gelatin phantom needs to be made for simulating the brain tissue scattering. It turns out that the gelatin with 50% of water and milk exhibits similar photoacoustic properties for brain tissue. Gelatin is made with 1/2 cold water dissolve first, then the 1/2 water and milk mixture is heated and add into the mixture. Then refrigerate it 3 hours till it's firm.

A. I. Farrer, H. Odéen, J. D. Bever, B. Coats, D. L. Parker, A. Payne, and D. A. Christensen, “Characterization and evaluation of tissue-mimicking gelatin phantoms for use with MRgFUS,” Journal of Therapeutic Ultrasound, vol. 3, no. 1, 2015.

battery-free wireless device

Ruochen Wang - Dec 11, 2019, 2:42 PM CST

Title: Fully implantable, battery-free wireless optoelectronic devices for spinal optogenetics

Date: 11/28/2019

Content by: Ruochen

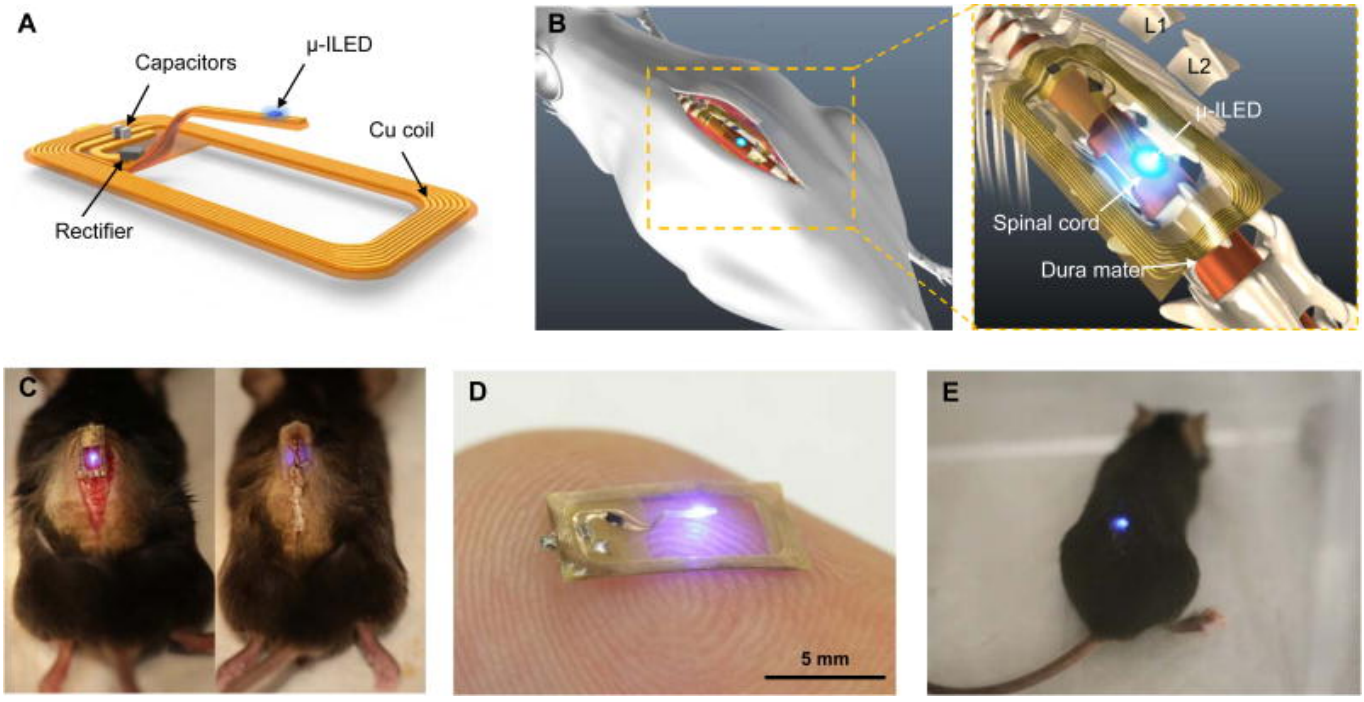
Content:

The overall device dimensions are 10 mm×5 mm×0.2 mm (L×W×thickness). The rectangular coil designated for wireless transmission consists of 7 planar loops with 50 μm pitch. The probe, equipped with a micro-inorganic light-emitting diode (μ-ILED; TR2227, Cree Inc. Raleigh, NC), stems inward from the 5 mm side of the coil, has a width of 400 μm, and is positioned centrally within the otherwise open-architecture device. The μ-ILED emits 470 nm blue light and has dimensions of 220 μm×270 μm×50 μm (L×W×thickness).

The transmission coil and needle are composed of a copper, polyimide, copper trilayer (Cu/PI/Cu, 18/50/18 μm thickness, Paralux, Dupont, Dover, DE). The top and bottom Cu layers are bridged through the introduction of 3 laser-drilled holes (50 μm in diameter), which are later filled with conductive silver paste.

The transmission coil and probe are defined through standard photolithography techniques, followed by utilization of a UV laser cutting tool (ProtoLaser U4, LKPF, Germany) to remove excess PI. The electronics that support wireless power transfer capabilities include a capacitor (40 pF, 250R05L220GC4T, Murata electronics, Japan), and a Schottky diode (CBDQR0130L-HF, Comchip Technology, Freemont, CA). The aforementioned components, along with the μ-ILED, are affixed to interconnect points through the use of solder paste. Finally, the optoelectronic device is encapsulated with poly(isobutylene) (PIB; ca. 30 μm thickness, BASF, Southfield, MI) followed by poly(dimethylsiloxane) (PDMS; ca. 10 μm thickness, Sylgard 184, Dow, Freeport, TX).

Both layers are generally formed by dip-coating (PIB conc. 8% in heptane, PDMS mixed at 10:1 ratio) with respective drying or curing at 70 °C.



It has integrated the whole circuit to the light, while our group design is to move the control circuit outside the mice's body.

They have tested the temperature with operating, at an extreme condition, with continuous operation at an output power of 50 mW/mm^2 in air, the maximum temperature increment from baseline was 1.7 °C.

This circuit is close to our group design in the basic idea but is smaller and flexible.

design idea sketch

Ruochen Wang - Oct 09, 2019, 11:20 AM CDT

Title: Design Idea Sketch

Date: 9/16/2019

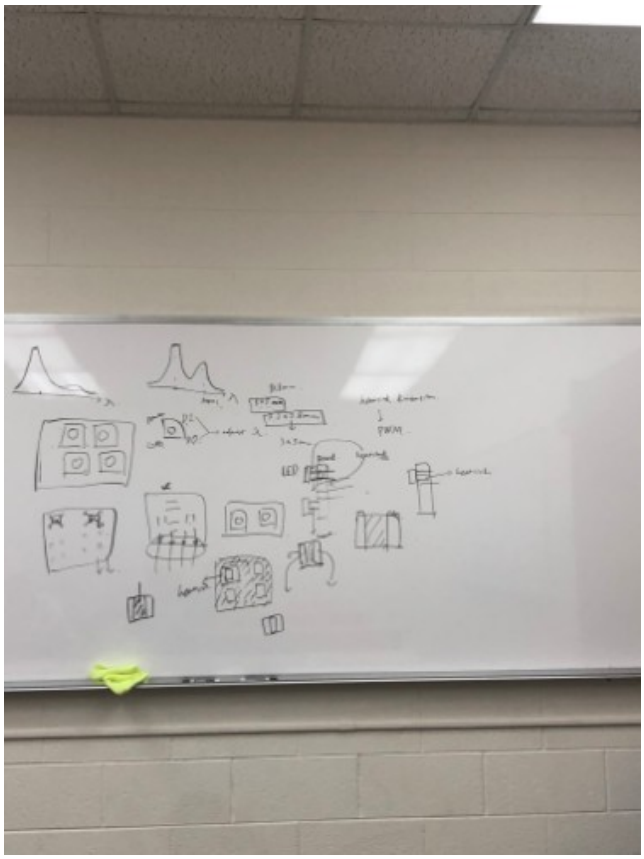
Content by: Ruochen

Present: Ruochen

Goals: To roughly design an overall sketch of the design

Content:

We had a team meeting, where we all exchanged our ideas. There are sketches about the roughly spectrum of the LEDs, the past design and the current proposed design with PCB. We discussed about potential probability where to put the heat diffuser.



Conclusion:

The PCB approach seems promising, and where to put a heat diffuser is tricky which we need to rethink about.

Ruochen Wang - Sep 16, 2019, 6:10 PM CDT

Circuit Schematics Design

Ruochen Wang - Oct 09, 2019, 11:15 AM CDT

Title: Circuit Schematics Design

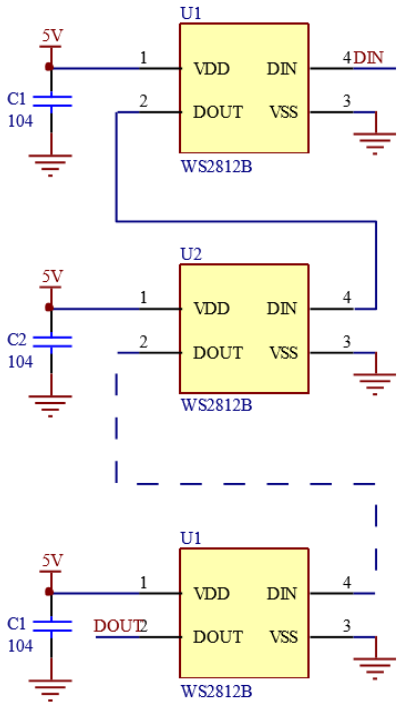
Date: 9/20/2019

Content by: Ruochen

Present: Ruochen

Goals: To roughly design an overall sketch of the circuit scheme

Content:



Conclusions/action items:

Putting all the LEDs into series so that all the LEDs could function as usual. Even though putting LEDs in parallel grants the same voltage for it to stay on the threshold.

Running a series circuit helps to provide the same amount of current to each LED. This means each LED in the circuit will be the same brightness and will not allow a single LED to hog more current than another. When each LED is receiving the same current it helps eliminate issues like thermal runaway.

The less heat it generates, the better it helps the project.