Organic LEDs as neuronal interfaces

Caroline Murawski

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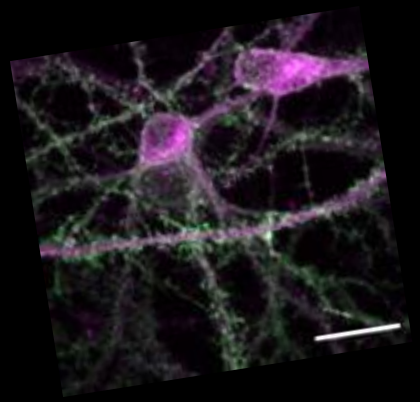

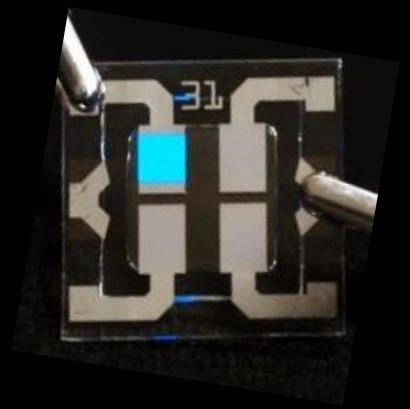

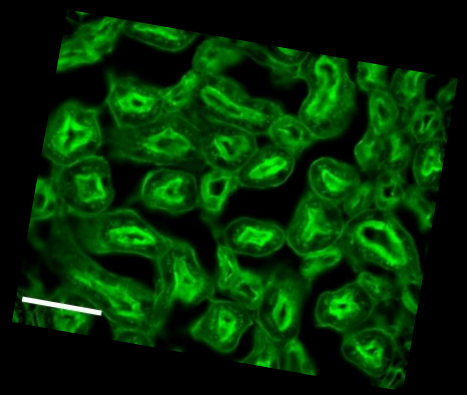

Chair of Nanotechnology, TU Dresden

21 Jan 2021

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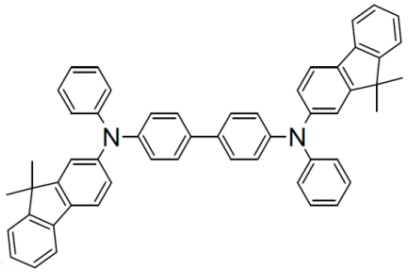
Main technologies:

- Electrochemical sensing
- Solid state electrolyte sensing
- Biophysical sensing
- Organic electronics

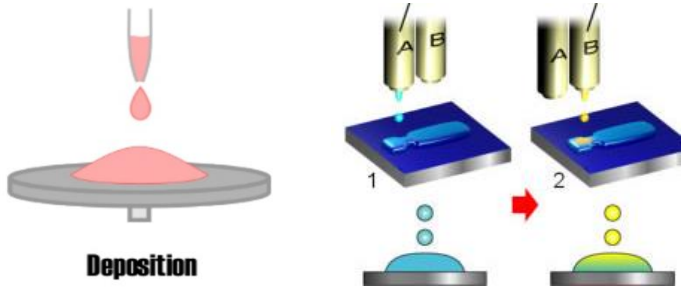
Applications:

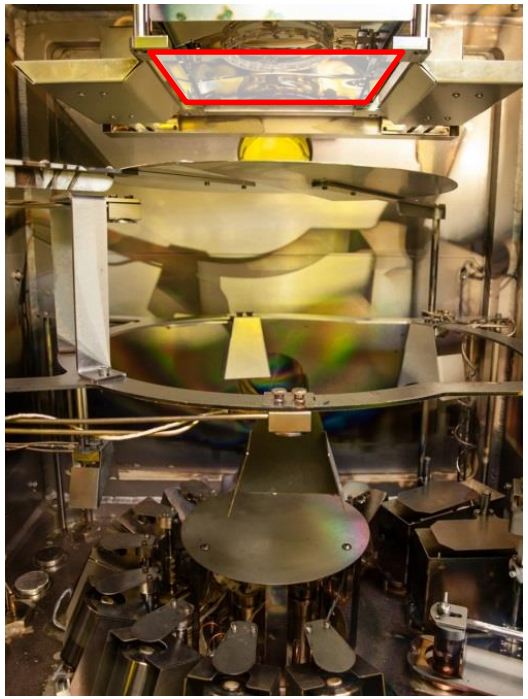
- Environmental sensing (water pollutants, agriculture)
- Gas sensors for biogas plants, hydrogen storage
- DNA origami for measurement of antigen/antibody binding
- Sensing of drugs in waste water
- Neural interfaces, functional implants

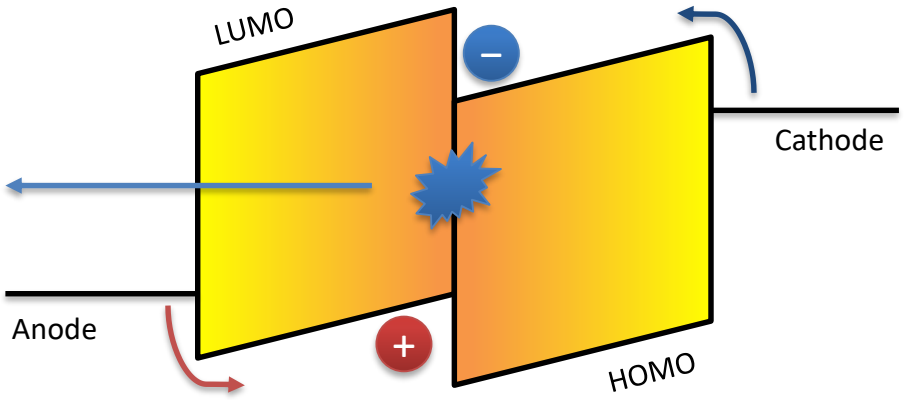
Organic LEDs

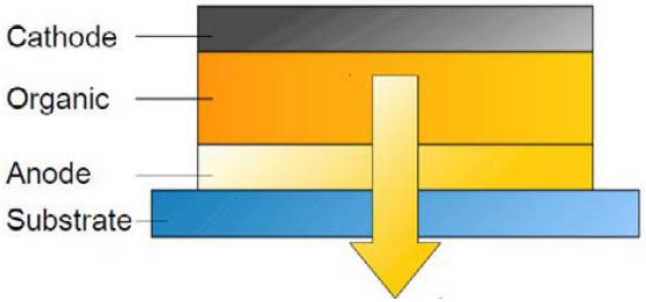


Fabrication



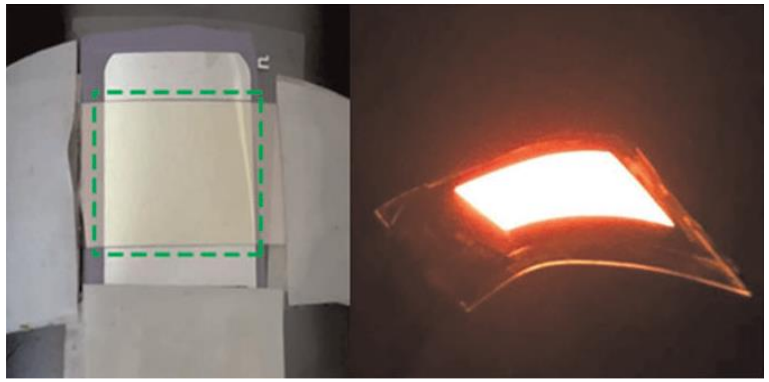






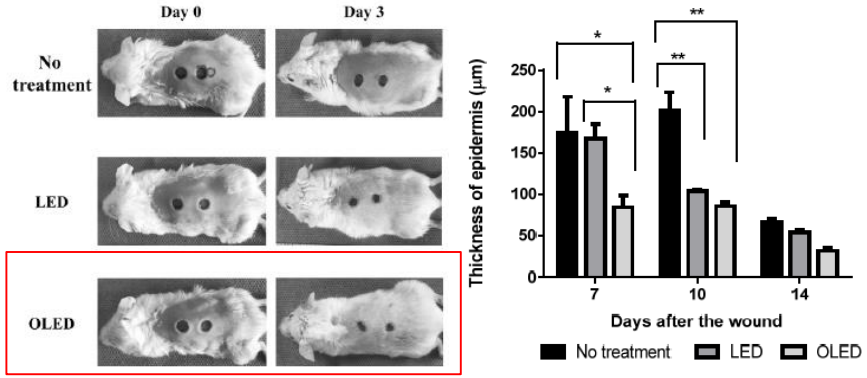
OLEDs for Biophotonics Applications

Photodynamic therapy



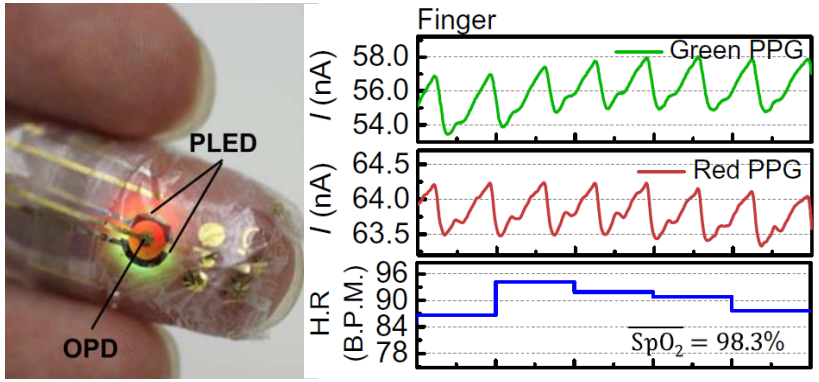
C. Lian, … I. D. W. Samuel, *npj Flex. Electron.* **2019**, *3*, 18.
S. K. Attili, … J. Ferguson, *Br. J. Dermatol.* **2009**, *161*, 170.

Photobiomodulation

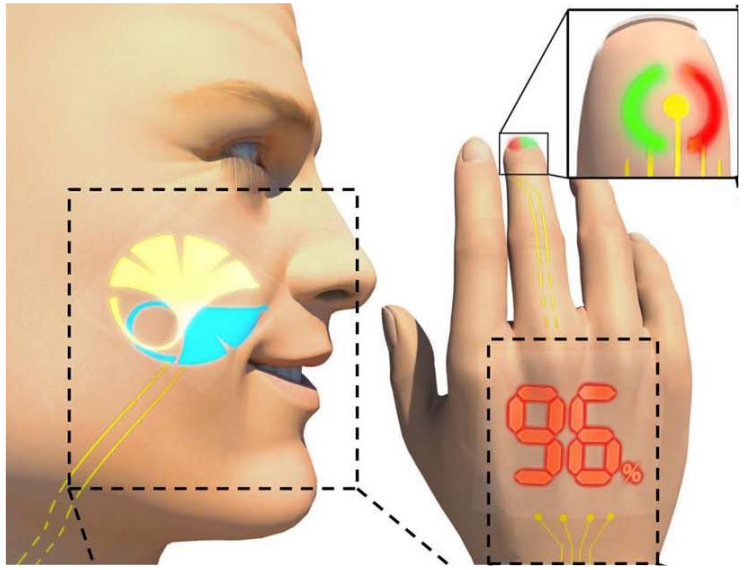


S. Mo, … J. C. Ahn, *Curr. Opt. Photonics* **2019**, *3*, 485.
Y. Jeon, … K. C. Choi, *Adv. Mater. Technol.* **2018**, *3*, 1.

Pulse oximetry



C. M. Lochner, … A. C. Arias, *Nat. Commun.* **2014**, *5*, 5745.
T. Yokota, … T. Someya, *Sci. Adv.* **2016**, *2*, e1501856.
H. Lee, … S. Yoo, *Sci. Adv.* **2018**, *4*, eaas9530.



On-skin applications

Flexible, wearable displays

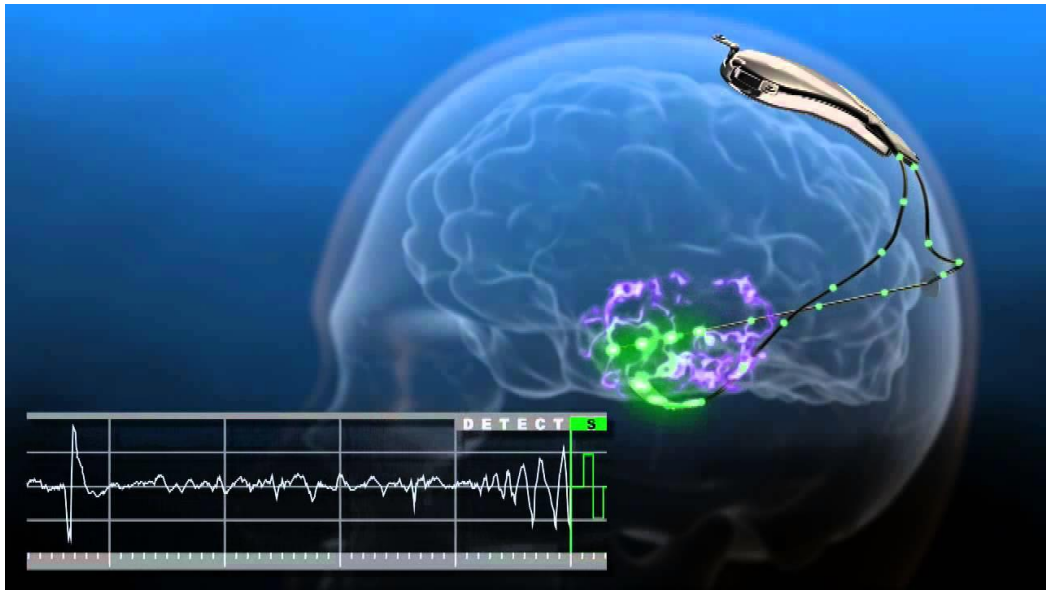
T. Yokota, … T. Someya, *Sci. Adv.* **2016**, *2*, e1501856.

Neurological Diseases

- More than 1 billion people affected world wide (WHO, 2006)
- Alzheimer‘s disease, epilepsy, migraine, …

How to control nerves?

- Pharmacology → not timely, not well targeted, many side effects
- Electrical stimulation → does not target specific cell type, no precise silencing

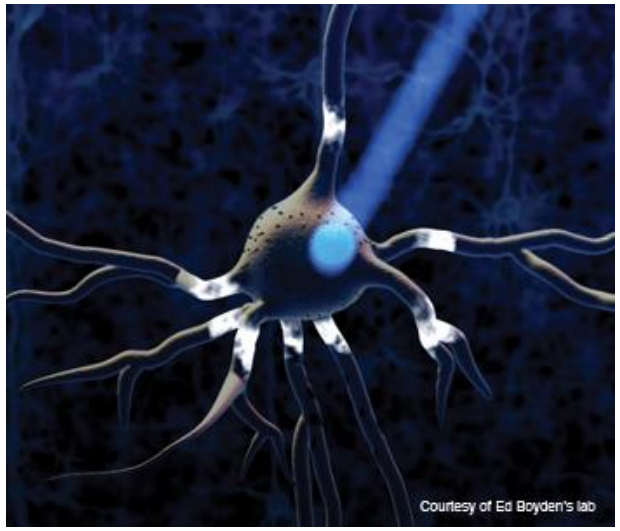


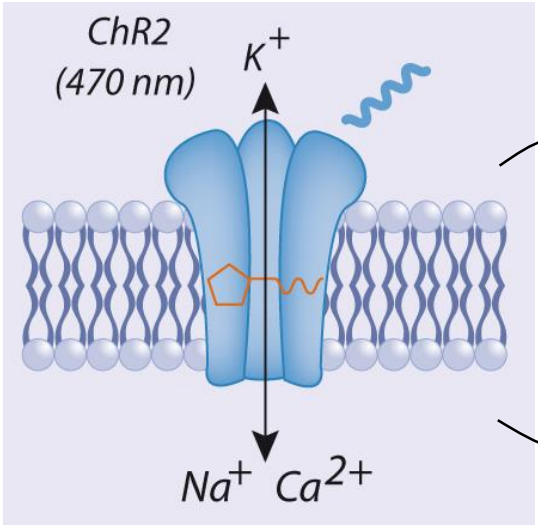
Epilepsy recognition and treatment device

NeuroPace, Inc.

Controlling Cells with Light

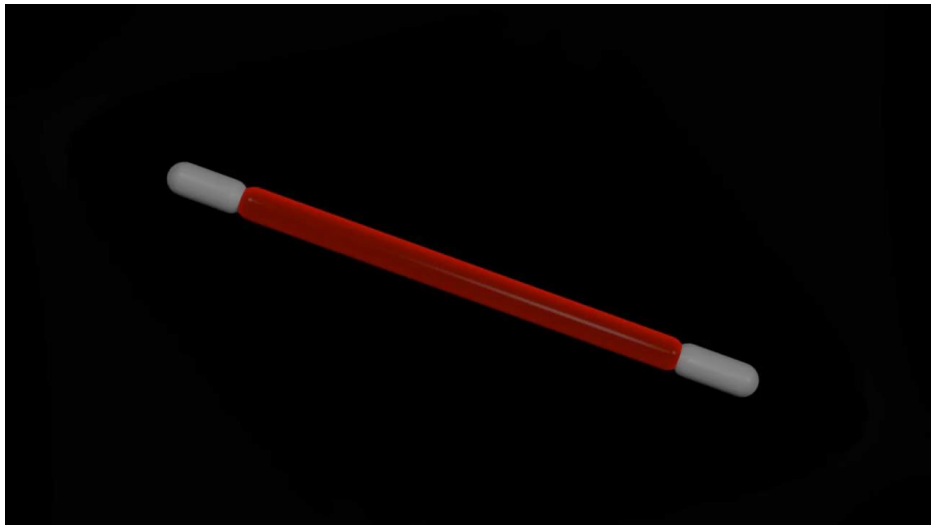
Optogenetics - artificial, genetically introduced light sensitivity





E. Pastrana, *Nat. Methods* **8**, 24 (2011)

Medical applications:



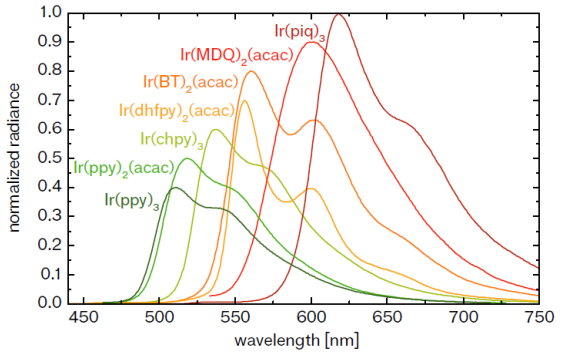
© Gensight Biologics:
Towards curing blindness
(retinitis pigmentosa)

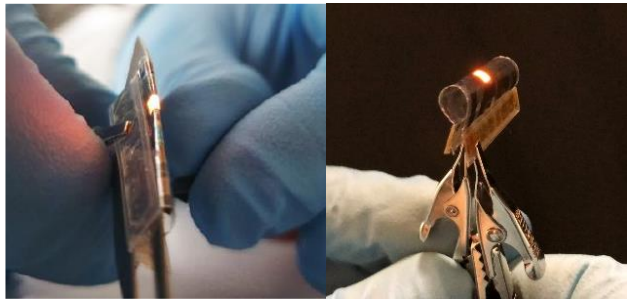
OLEDs for Optogenetics

Advantages of organic LEDs

- Structuring to high-density arrays with cell-scale dimensions
- High spectral control
- Biocompatibility/ Flexibility

COMEDD Fraunhofer





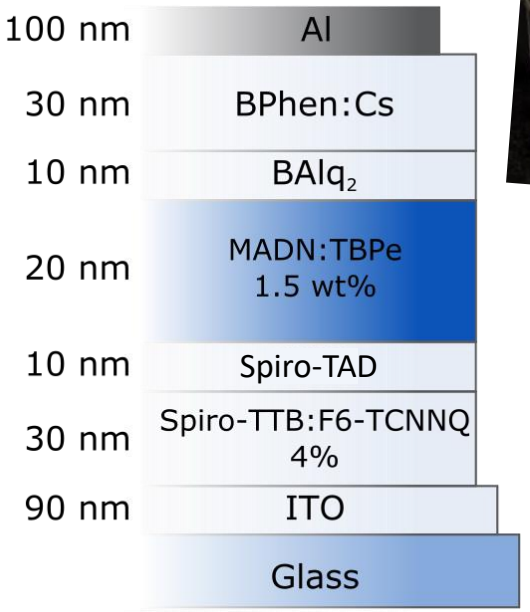
C.-M. Keum, C. Murawski *et al.*, *Nat. Comm.* **11**, 6250 (2020)

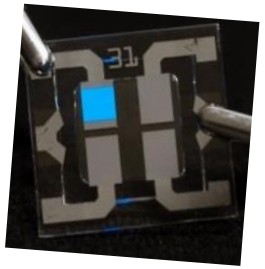
Requirements of OLEDs for optogenetics

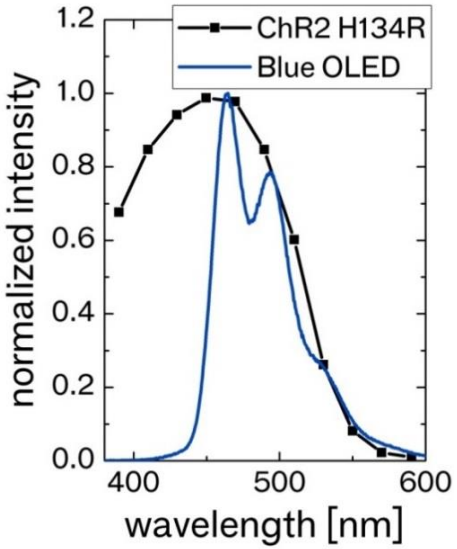
- Good spectral overlap of ChR activation and OLED emission
- Low temperature spreading onto cells
- High durability in aqueous environment
- High brightness necessary (≈ 0.1 – 10 mW/mm^2)

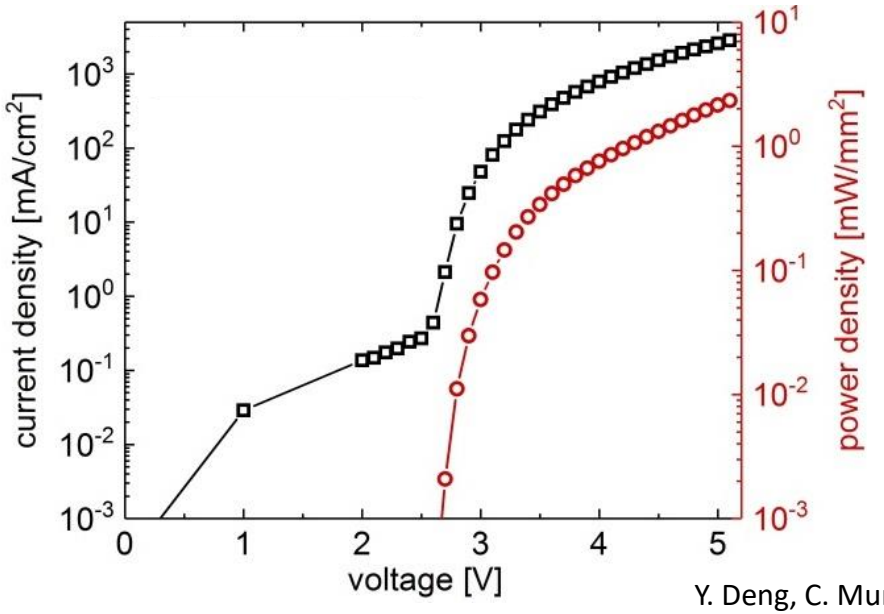
High-Brightness Performance

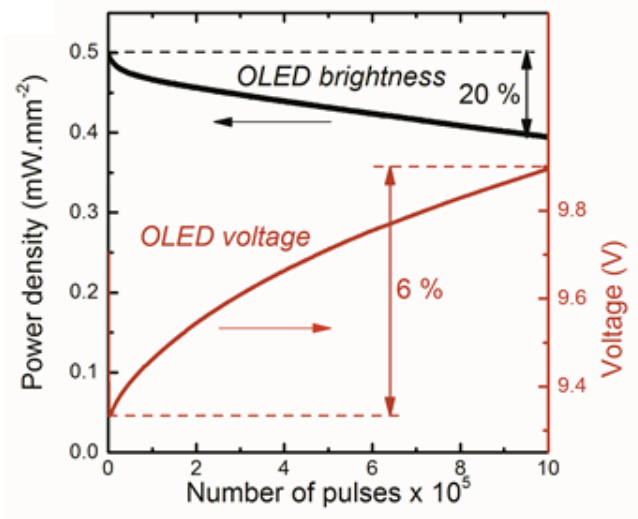
- Current microdisplays provide 0.001 – 0.01 mW/mm²
- For high-brightness illumination used fluorescent *pin*-OLEDs
- Low voltages required
- Low temperature spreading
- High stability over millions of pulses







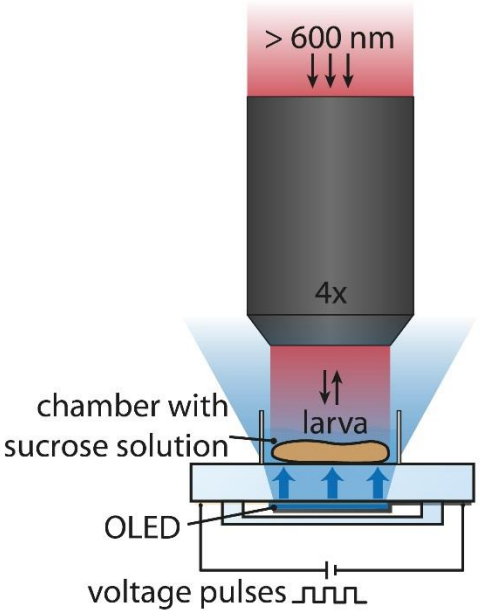


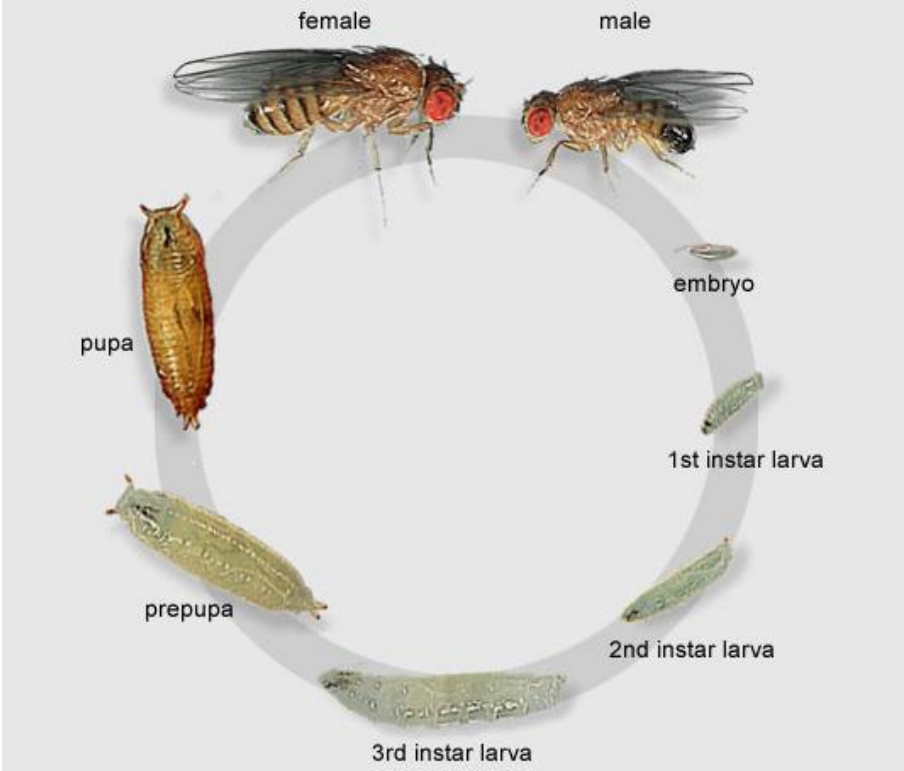


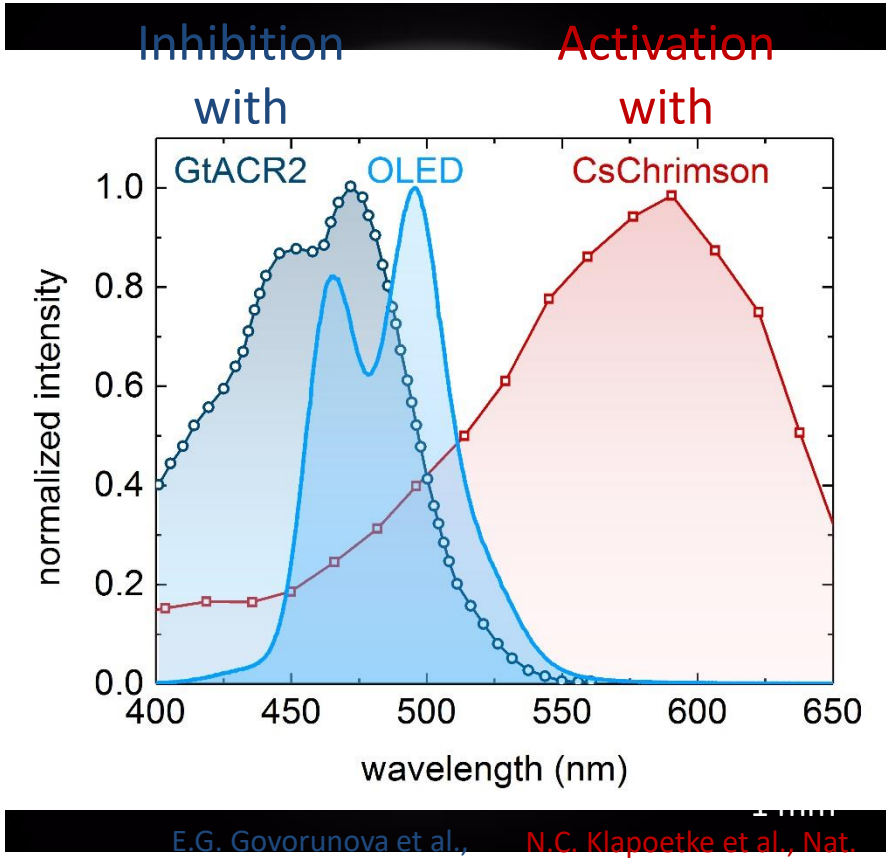
Y. Deng, C. Murawski et al., *Adv. Opt. Mater*. **8**, 1901721 (2020)
A. Morton, C. Murawski et al., *Adv. Biosyst*. **3**, 1800290 (2019)

Stimulating *Drosophila* Larvae

- Used *Drosophila* line expressing ChR2(H134R) in motor neurons (OK371-GAL4 driver)
- Firing of action potentials immobilizes the larva





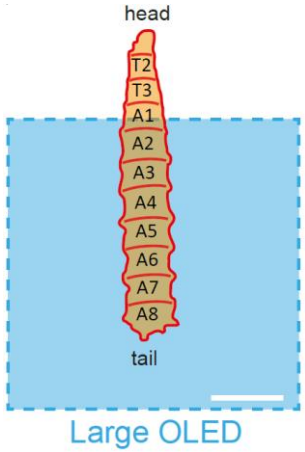


E.G. Govorunova et al., Science **349**, 647 (2015)

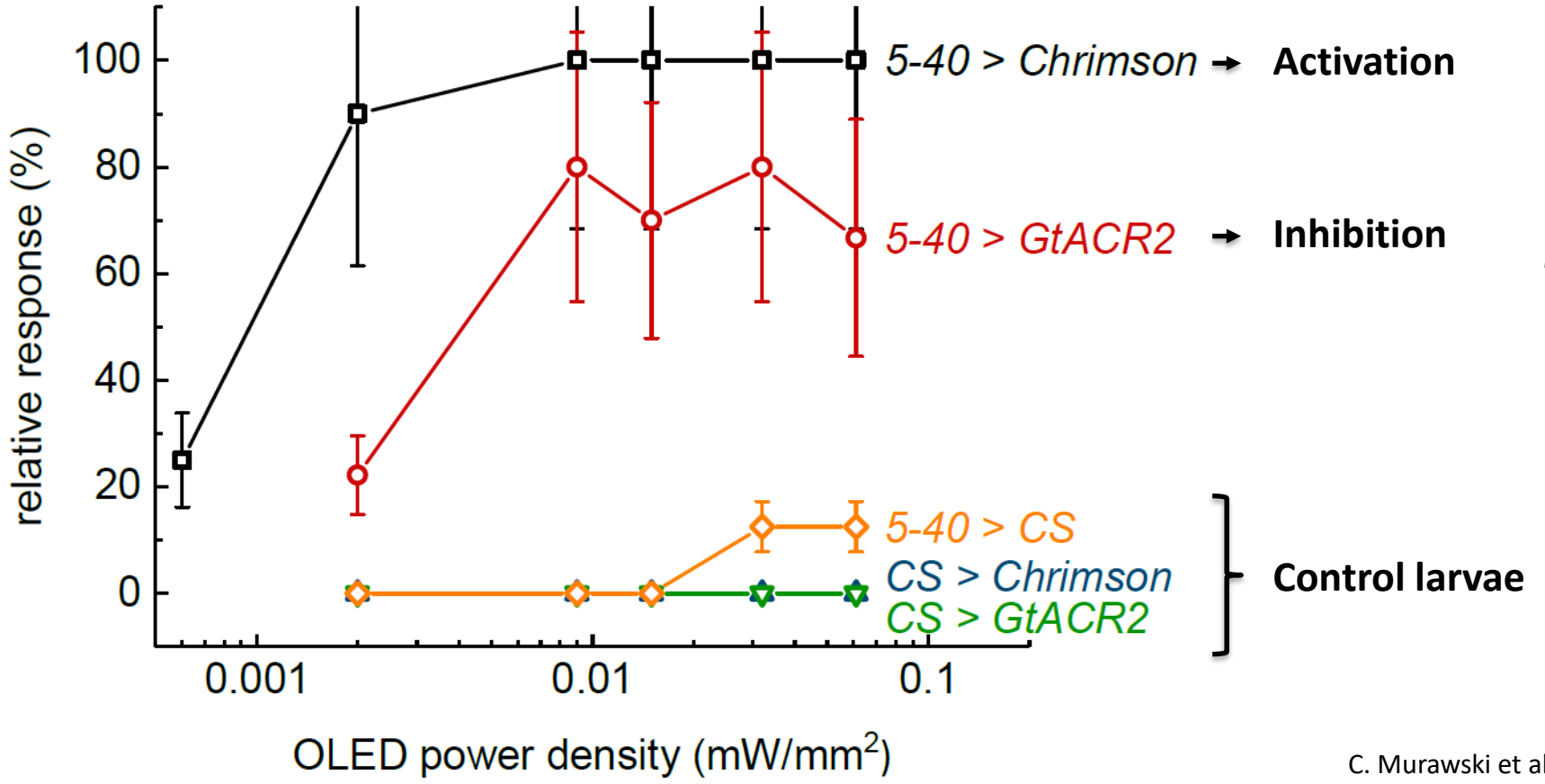
N.C. Klapoetke et al., Nat. Methods. **11**, 338 (2014)

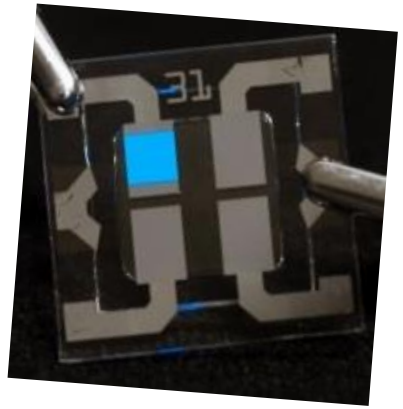
A. Morton, C. Murawski et al., *Sci. Rep*. **6**, 31117 (2016)
C. Murawski et al., in *Light. Energy Environ.* (OSA, 2016), p. JW4A.9

Dose Response Curve



Studied larval locomotion in response to stimulation of all sensory neurons (5-40-GAL4 driver)



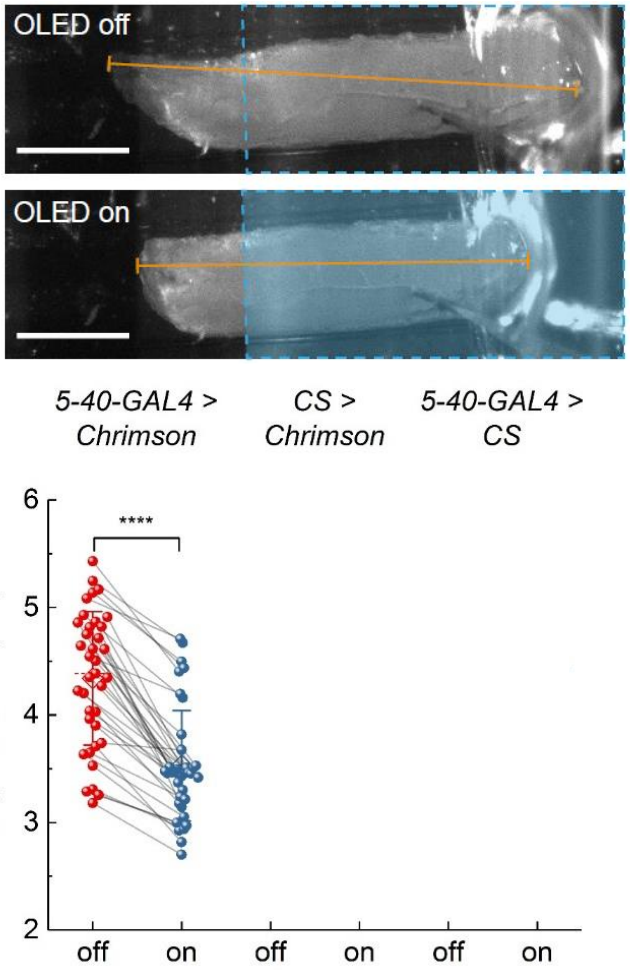


C. Murawski et al., *Nat. Comm.* **11**, 6248 (2020)

Response upon Global Stimulation

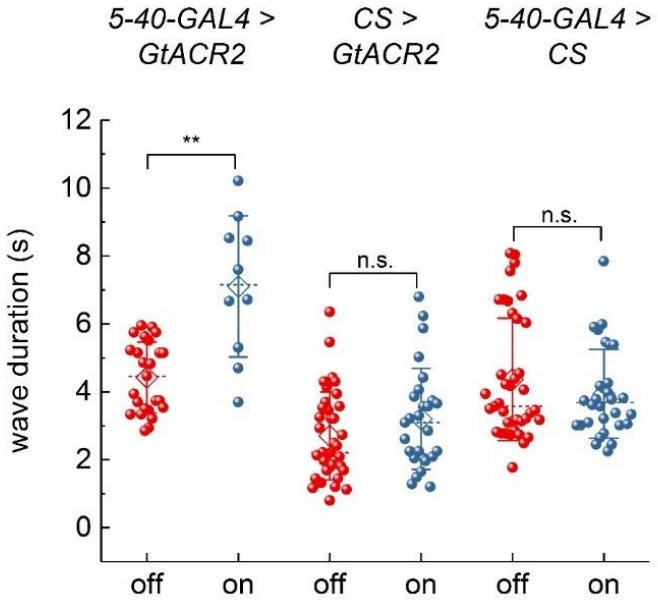
Activation of sensory neurons (Chrimson)

- Causes a full-body muscle contraction



Inhibition of sensory neurons (GtACR2)

- Causes slow-down of muscle contraction waves

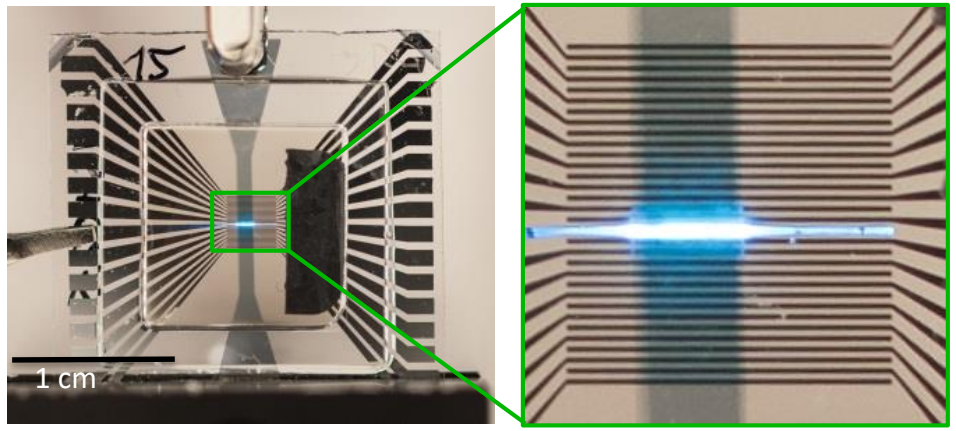


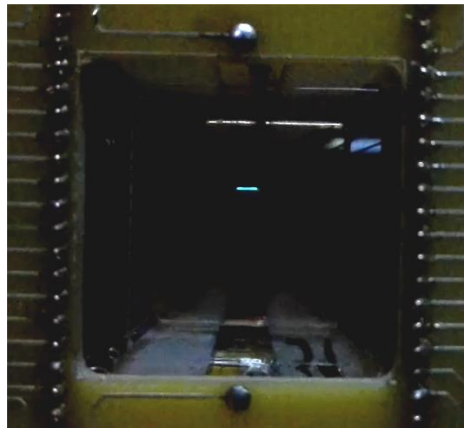
at 0.015 mW/mm^2

C. Murawski et al., *Nat. Comm.* **11**, 6248 (2020)

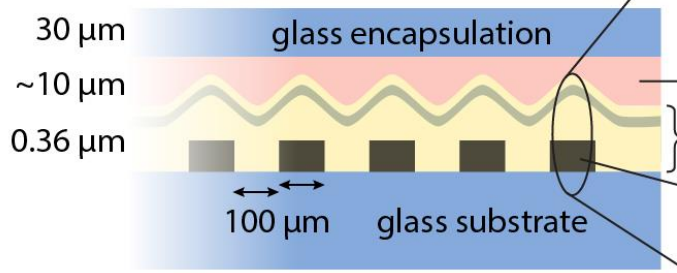
Structured Illumination

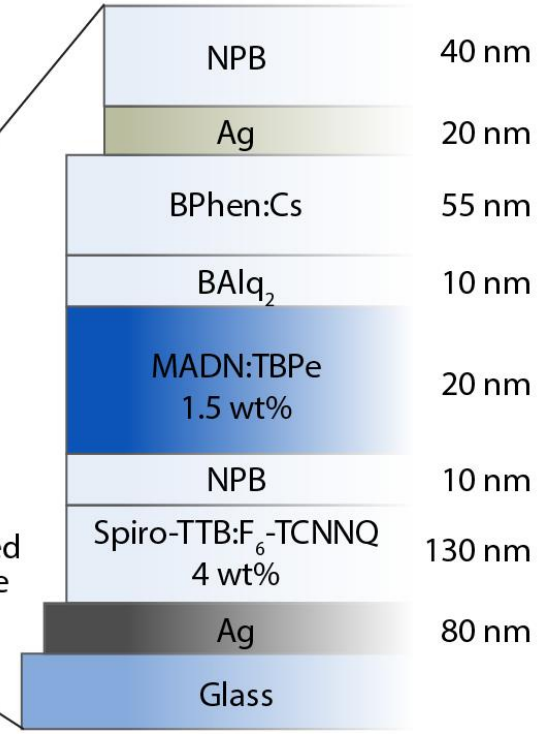
- Structured bottom electrodes with photolithography to 1D array with 10 – 100 µm pixel width
- Top-emitting OLED fabrication
- Encapsulated with 30 µm flexible glass sheet





Arduino driver operating 32 pixels

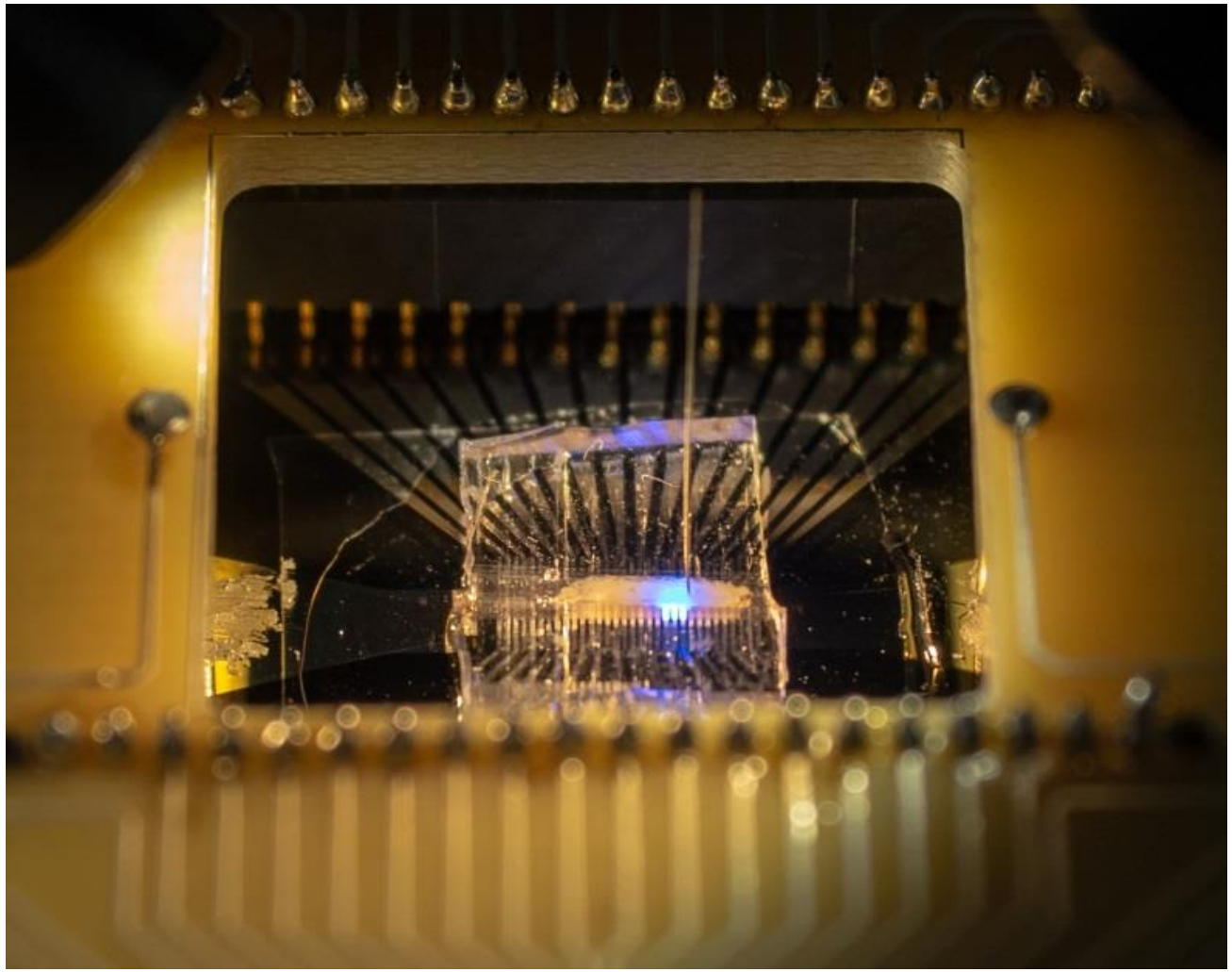


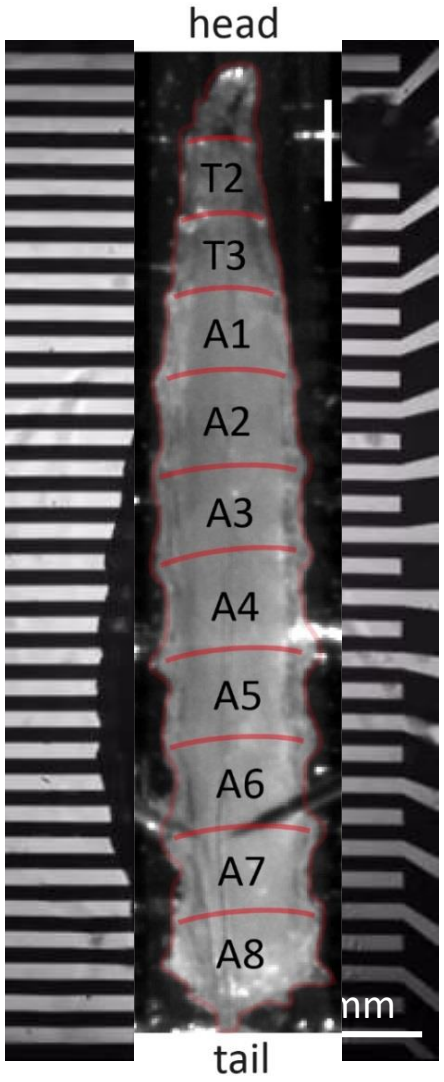


C. Murawski et al., *Nat. Comm.* **11**, 6248 (2020)

Segment-Specific Response

- Stimulation of individual segments → study behavioural response



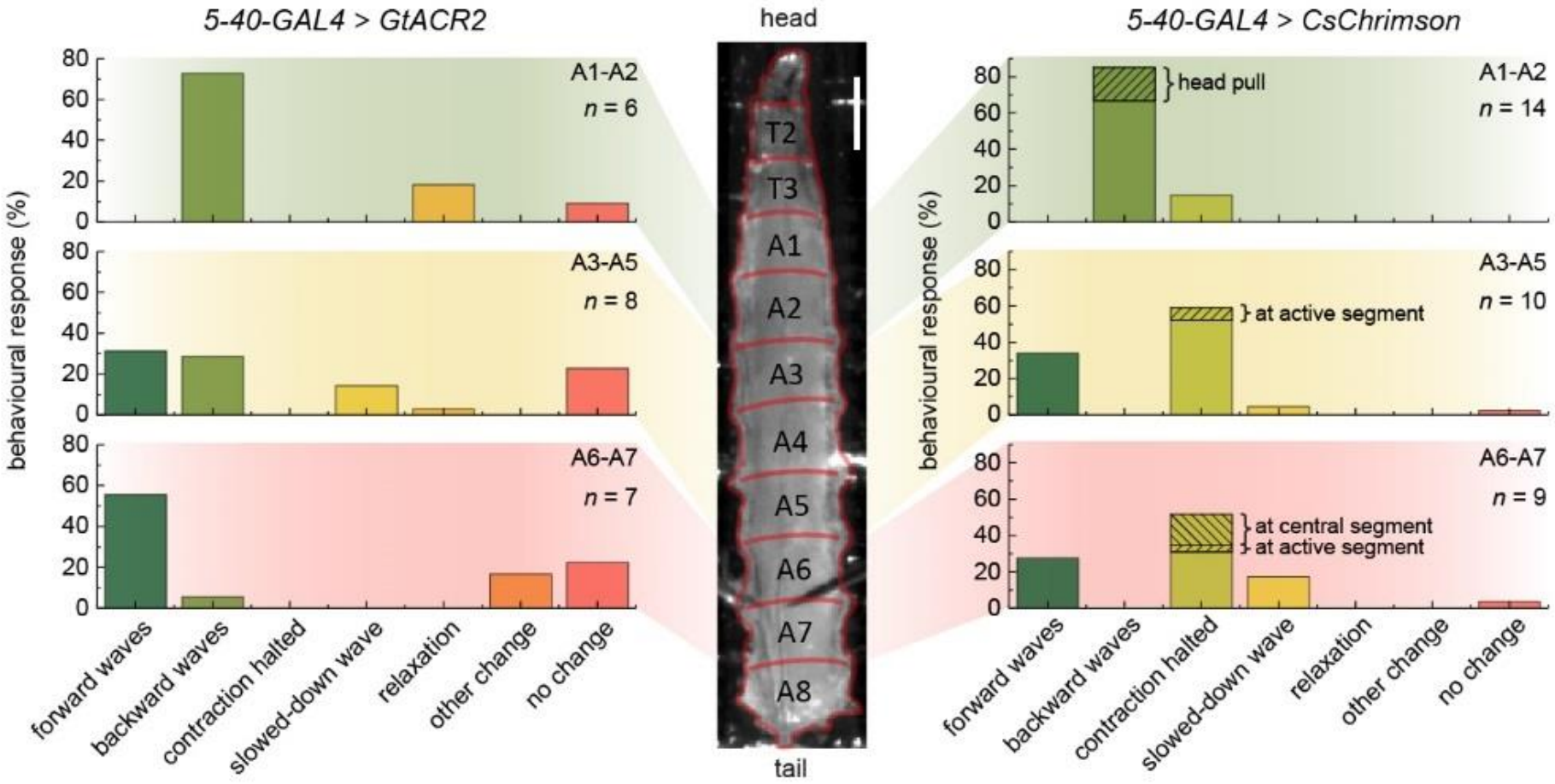


C. Murawski et al., *Nat. Comm.* **11**, 6248 (2020)

Behavioral Response to Local Stimulation

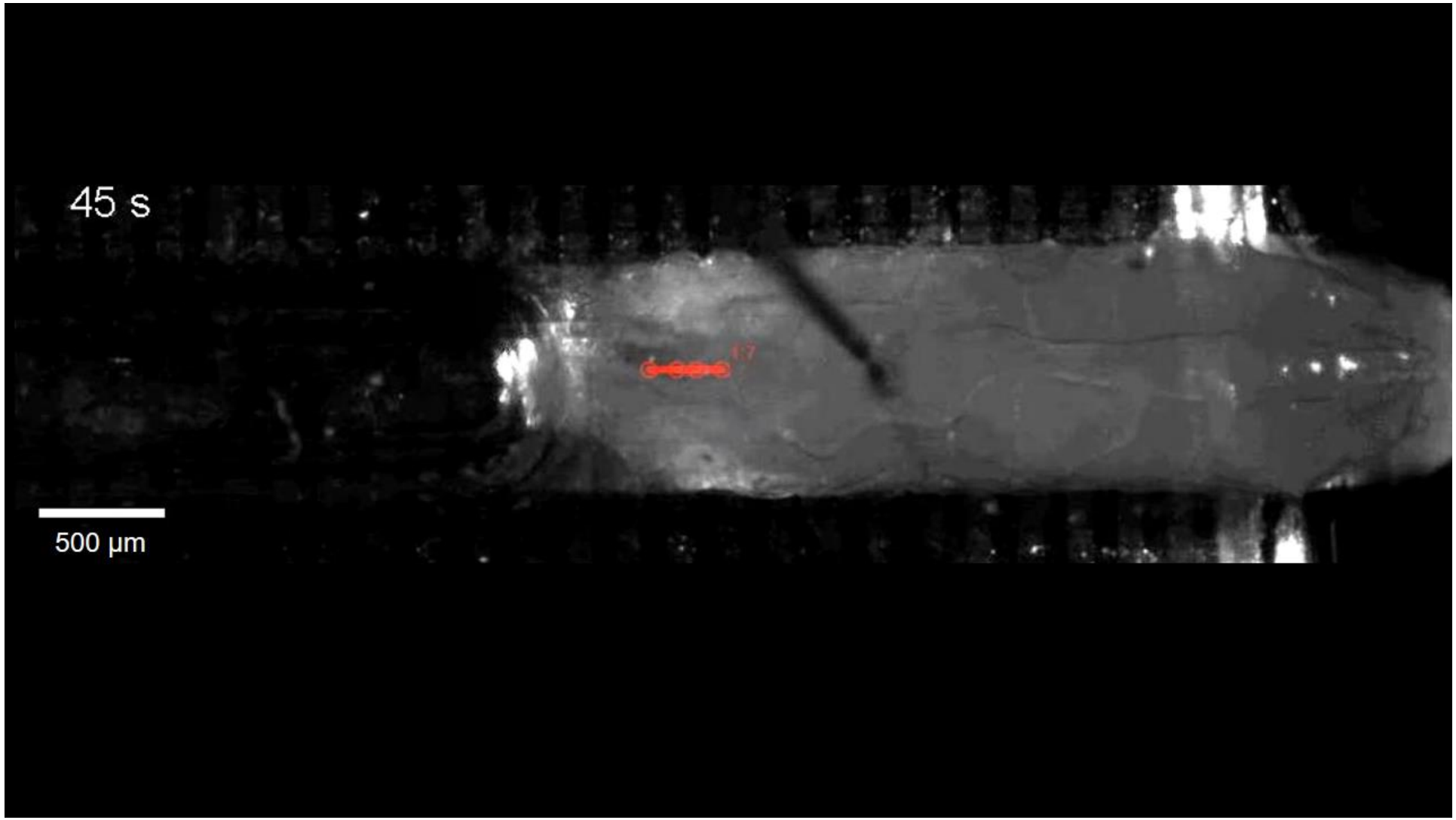
Inhibition

Activation



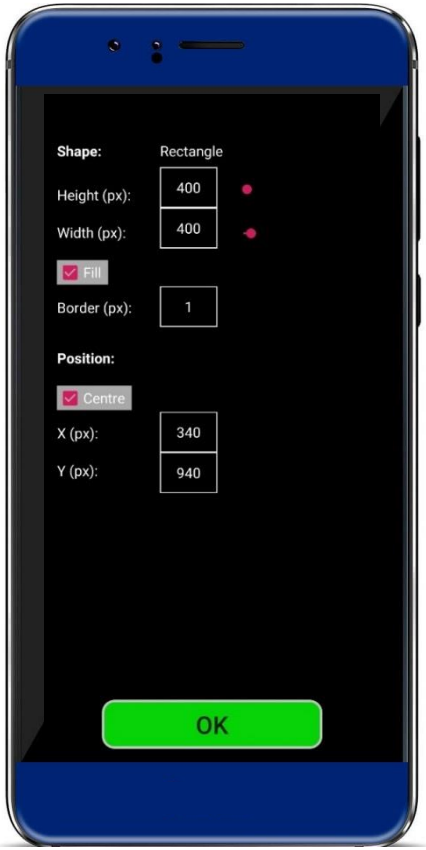
C. Murawski et al., *Nat. Comm.* **11**, 6248 (2020)

Switching Locomotion Direction

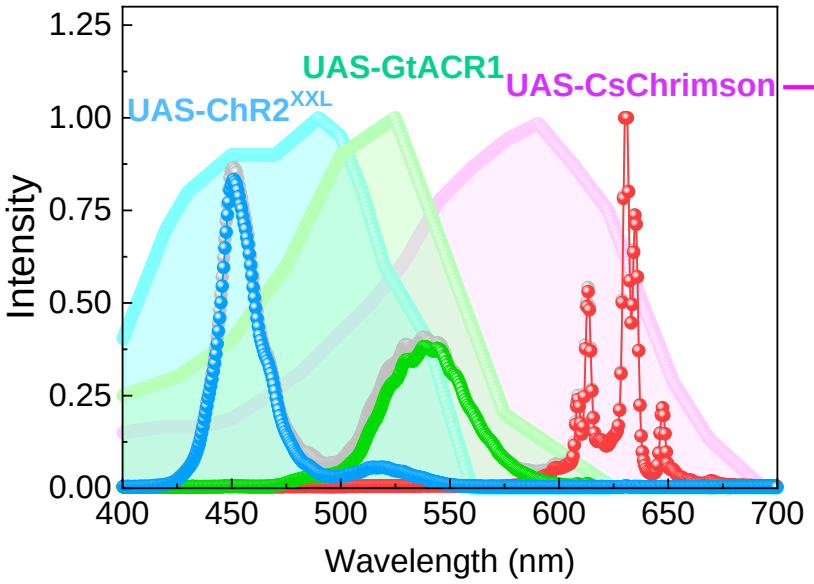


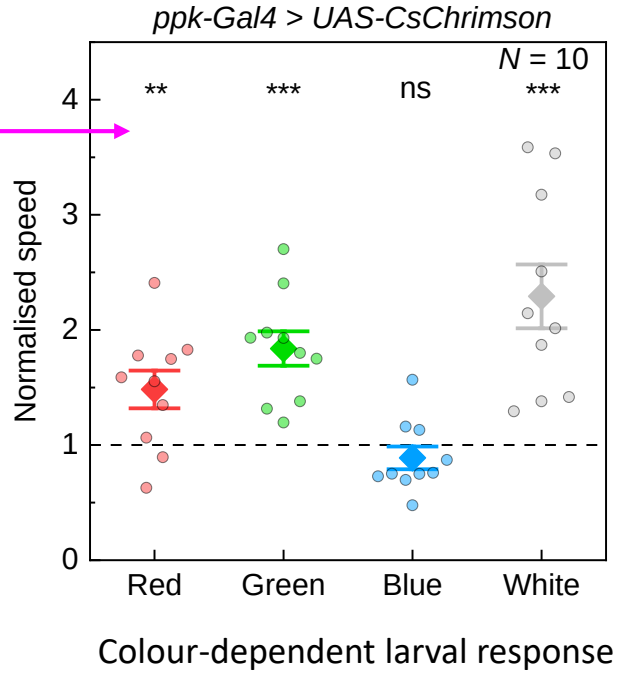
C. Murawski et al., *Nat. Comm.* **11**, 6248 (2020)

Smartphone Optogenetics



- Control behaviour or *Drosophila* larvae using smartphone display
- Observed significant light-response depending on colour and intensity of stimulation





Colour-dependent larval response

Ilenia Meloni

UNIVERSITÄT LEIPZIG

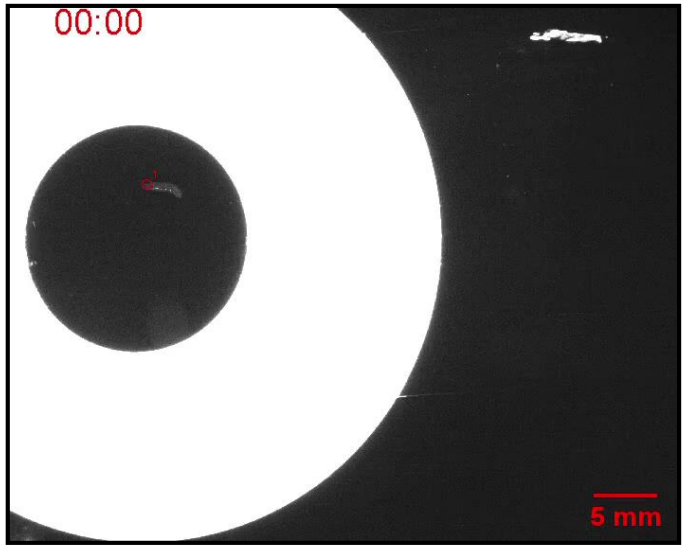
Andreas Thum, Robert Kittel

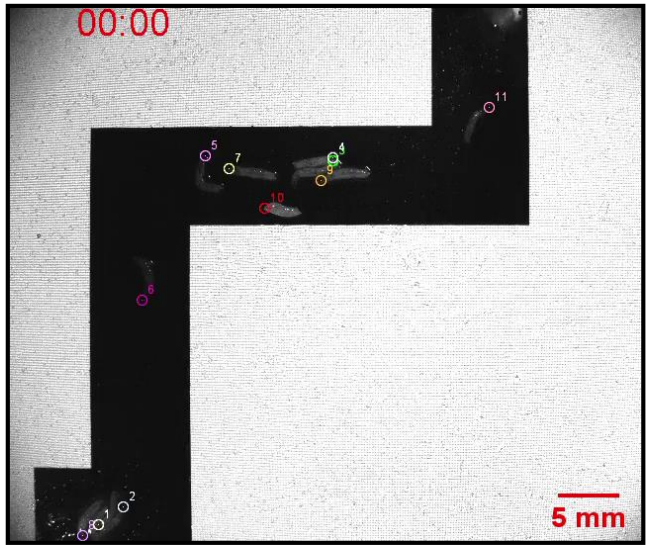
I. Meloni, …, C. Murawski, *Sci. Rep.* **10**, 17614 (2020)

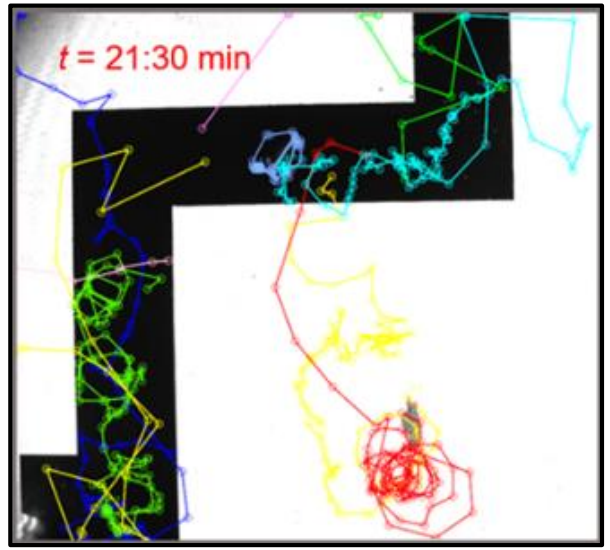
Smartphone Optogenetics

Drosophila larvae in a maze

Guiding larvae on the display







Ilenia Meloni

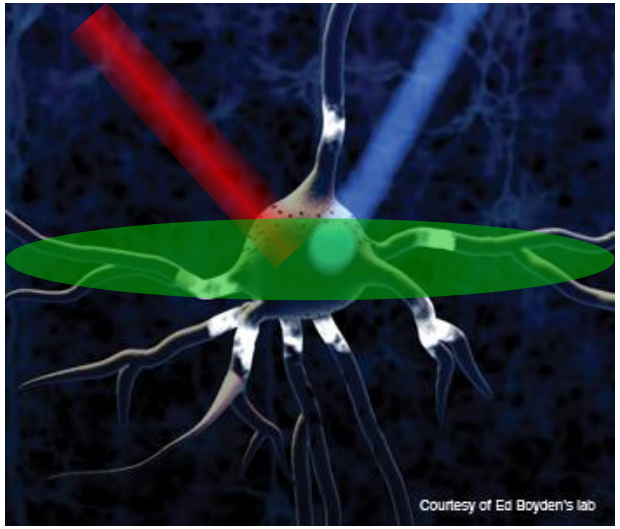
UNIVERSITÄT LEIPZIG

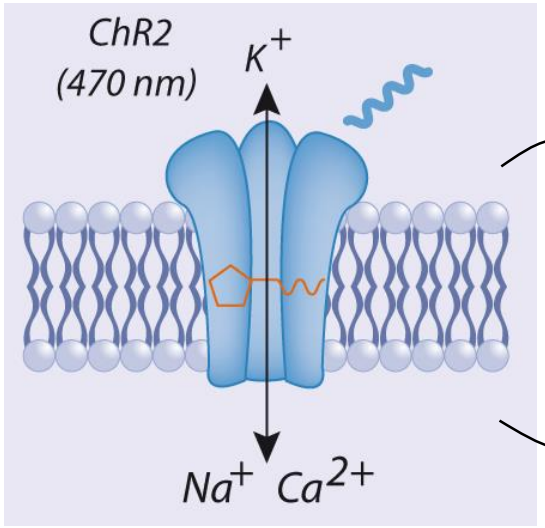
Andreas Thum, Robert Kittel

- Simple, high-resolution optogenetics to improve understanding of neuronal circuits
- Can be used to study learning and memory behaviour
- Suitable for teaching and outreach activities

I. Meloni, …, C. Murawski, *Sci. Rep.* **10**, 17614 (2020)

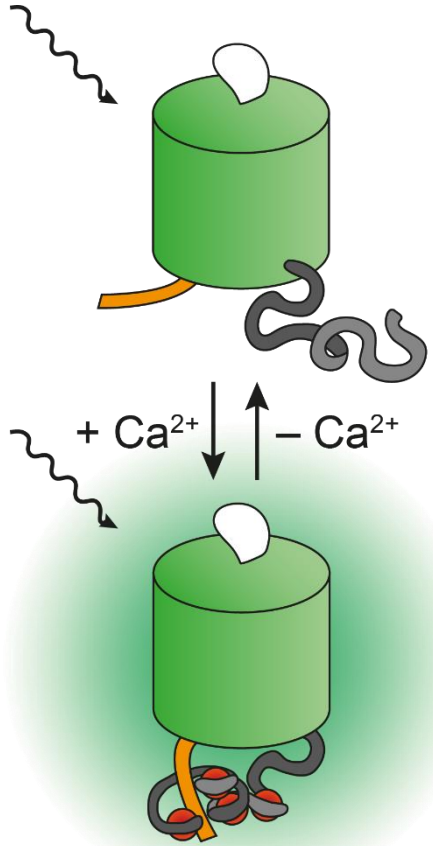
Optogenetics is more than only stimulation…





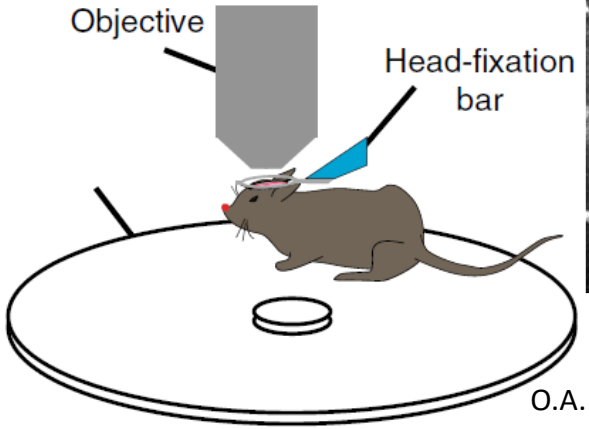
Membrane potential

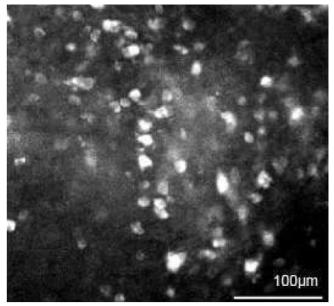
E. Pastrana, *Nat. Methods* **8**, 24 (2011)



… it also enables sensing neural activity with light

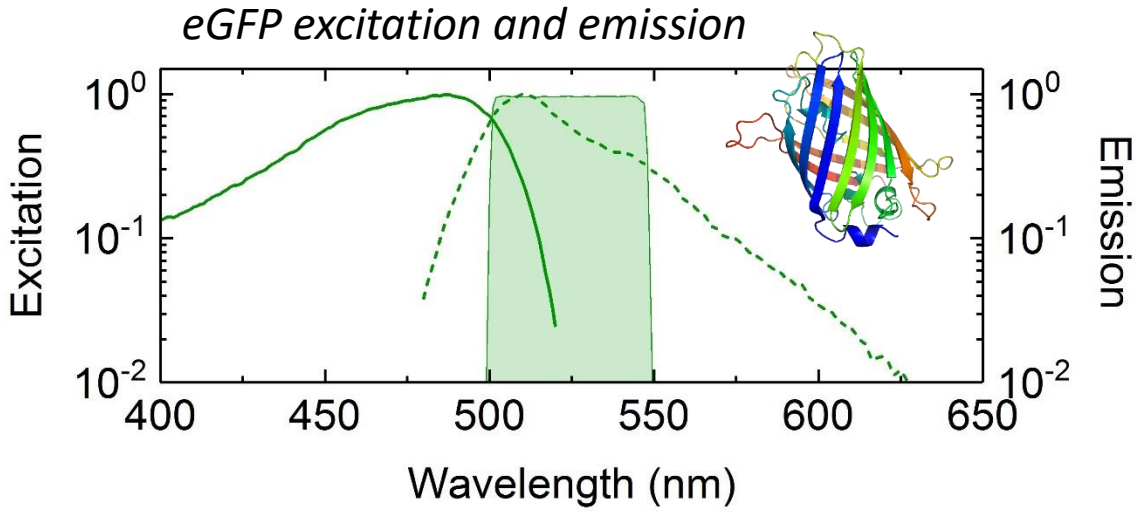
- Genetically encoded Calcium indicators
- Light intensity depends on Ca^{2+} concentration

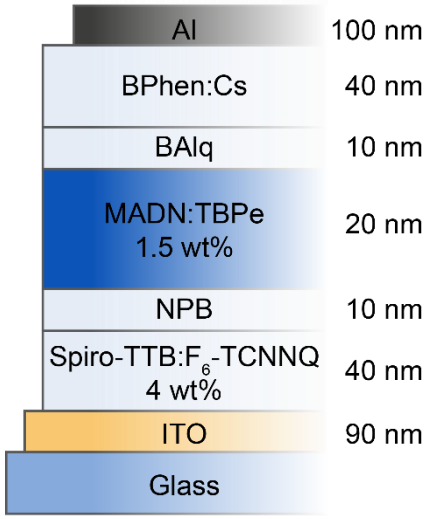


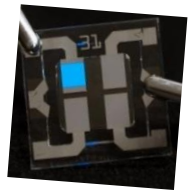


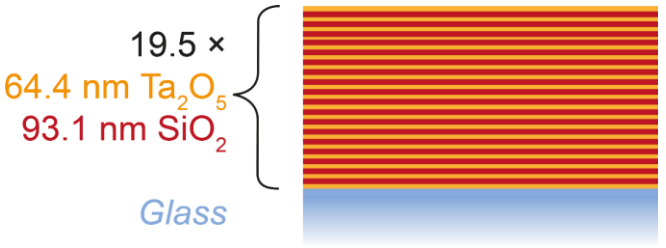
L. Ghanbari et al., *Nat. Comm.* **2019**, *10*, 1500.
O.A. Shemesh et al., *BioRxiv* **2019**, 10.1101/773069.

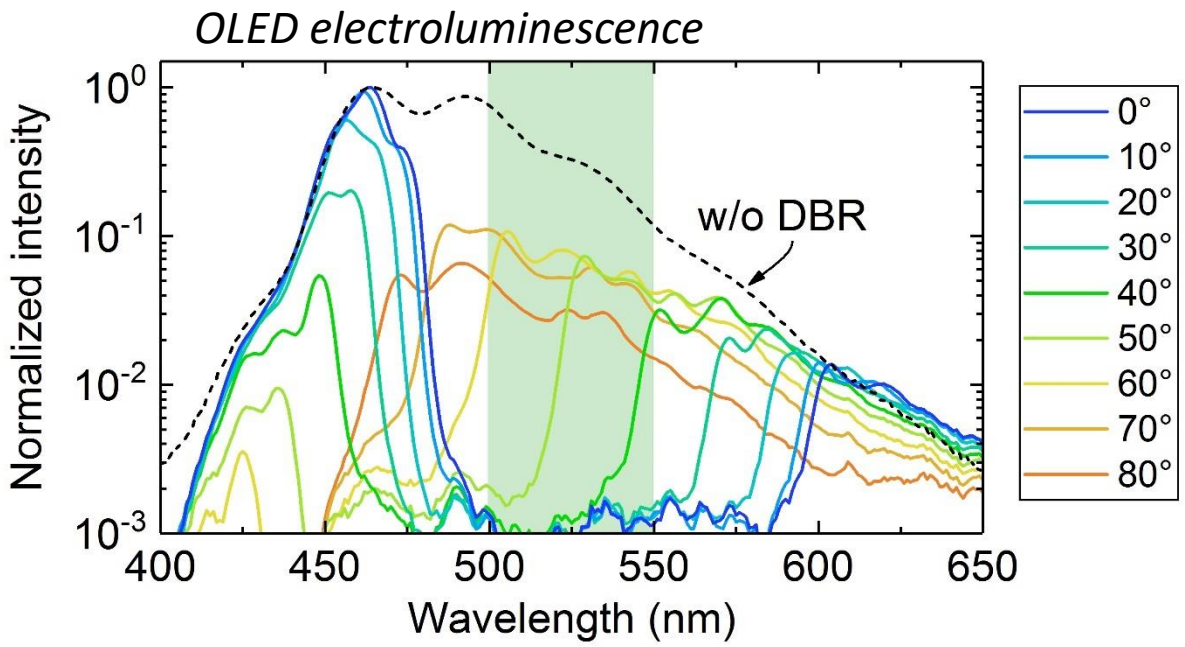
Device Design and Performance

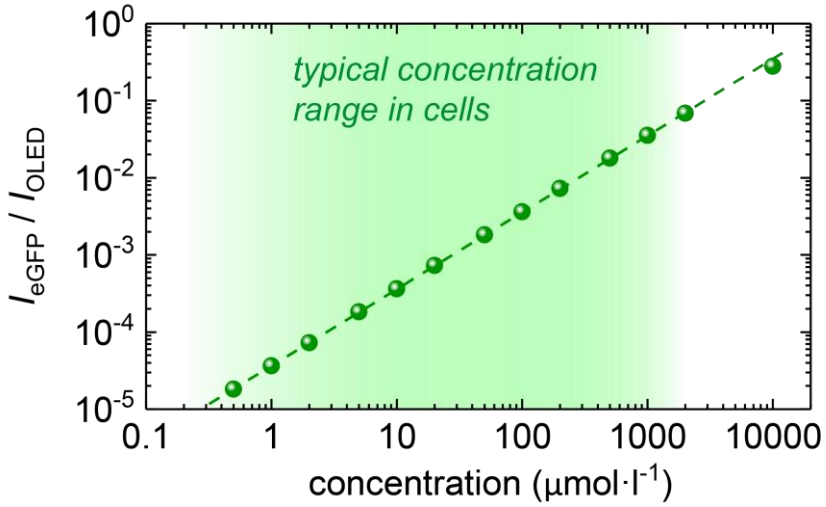










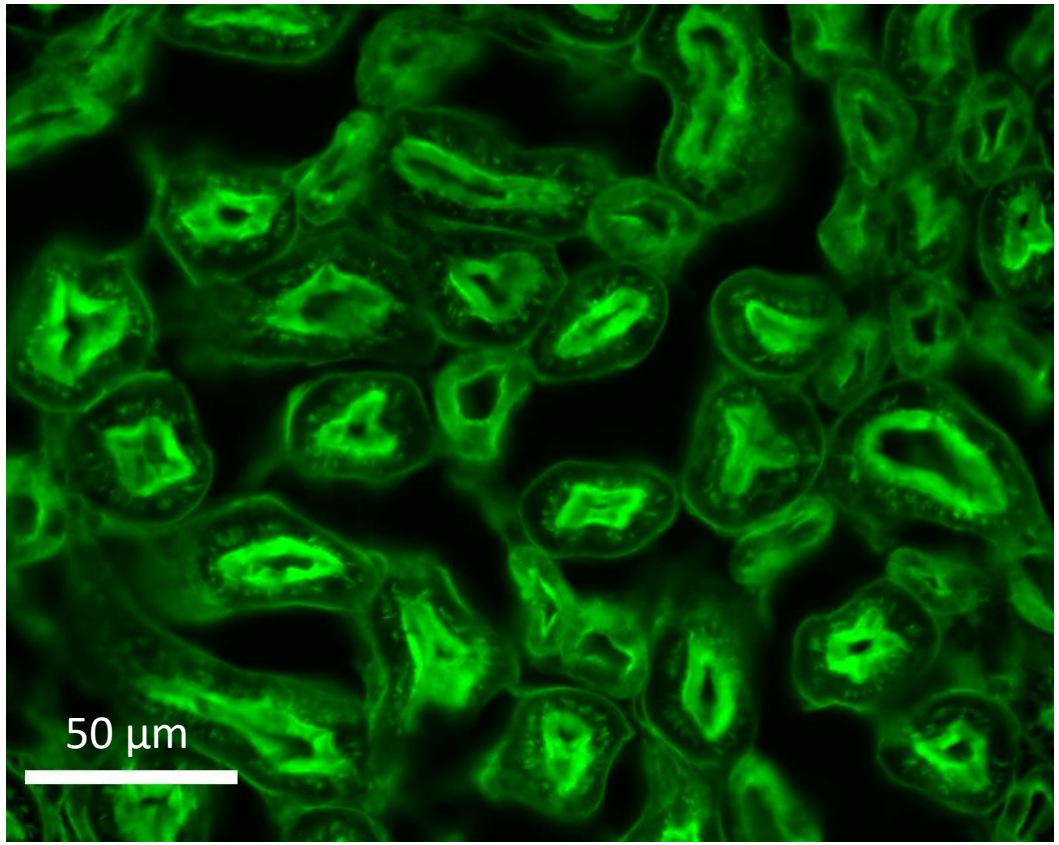


C. Murawski et al., *Adv. Mater.* **31**, 1903599 (2019)

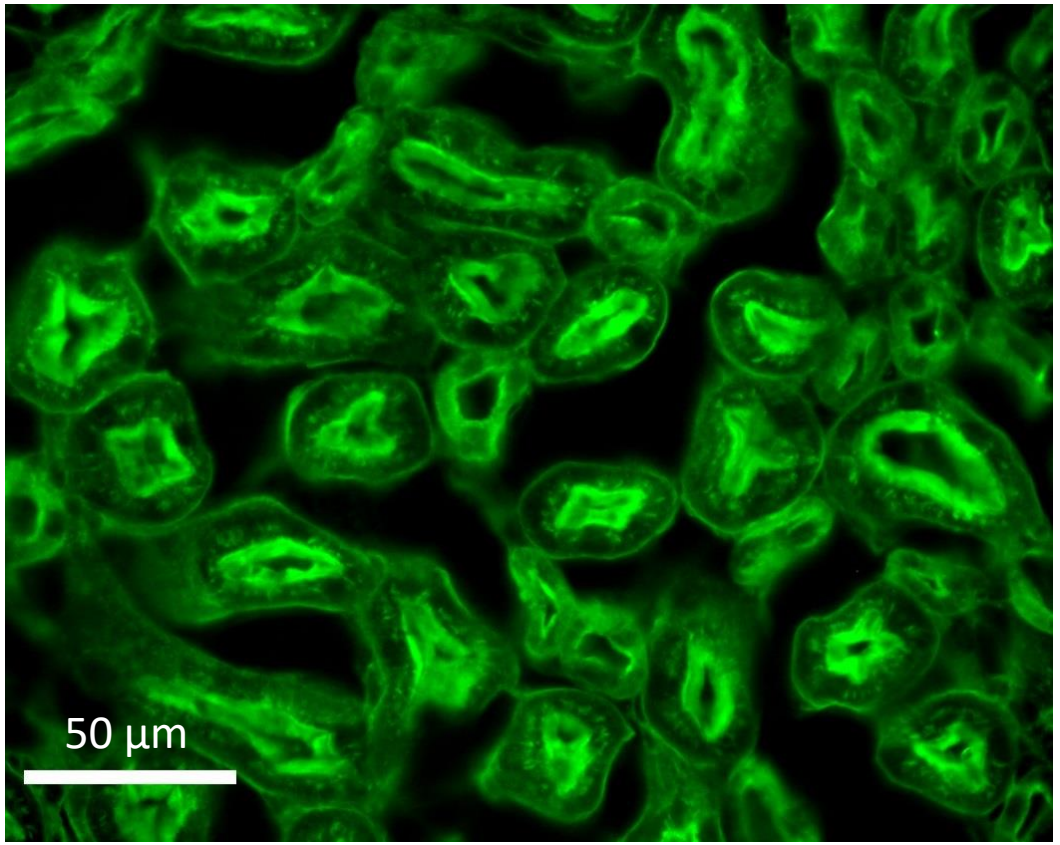
Fluorescence from Stained Cells

- Stained mouse kidney section
- Glomeruli labelled with Alexa Fluor® 488 wheat germ agglutinin

Mercury light source in epi-illumination



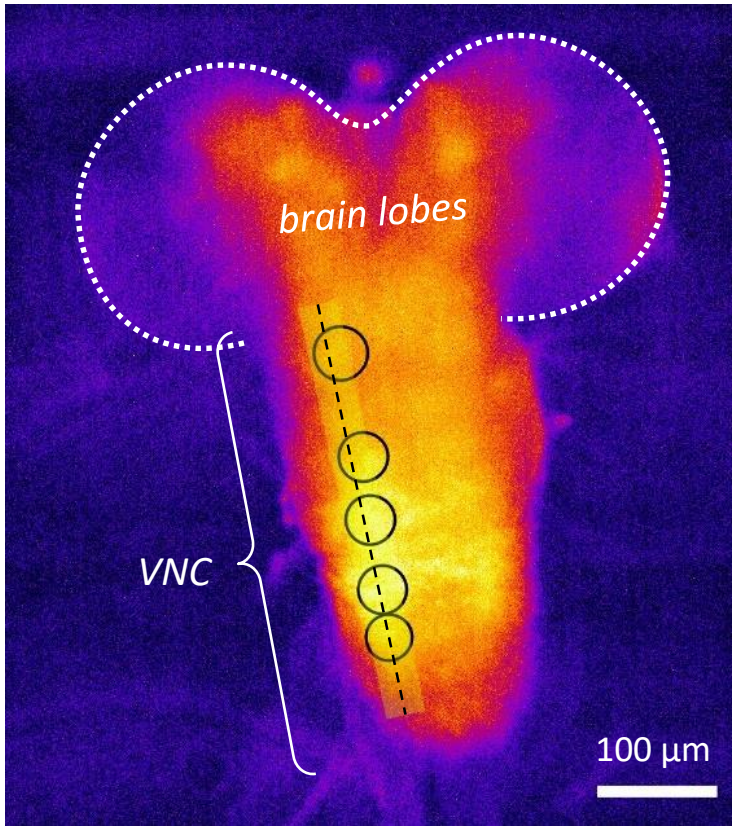
OLED illumination from below

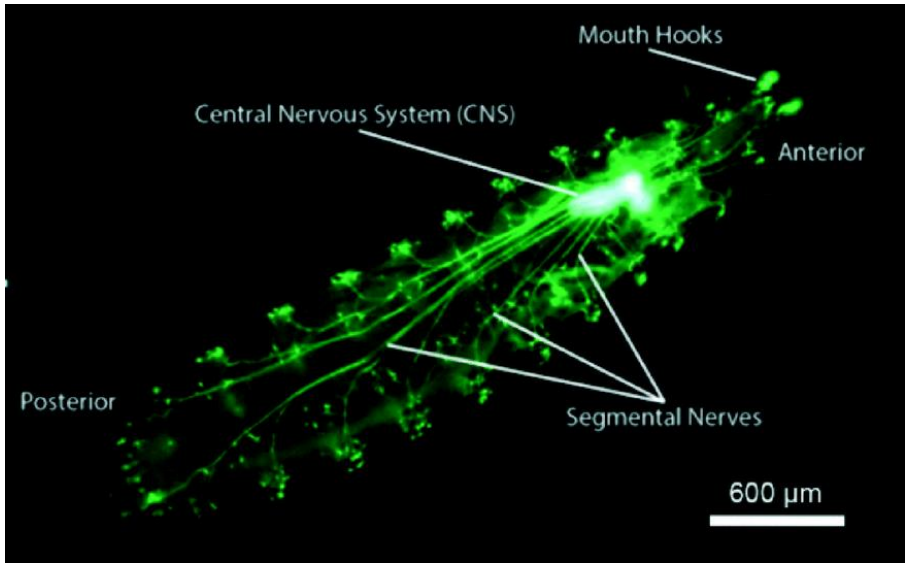


C. Murawski et al., *Adv. Mater.* **31**, 1903599 (2019)

Ca-Imaging of Neural Activity with OLEDs

Dissected CNS of *Drosophila melanogaster* larva with GCaMP6s in all neurons

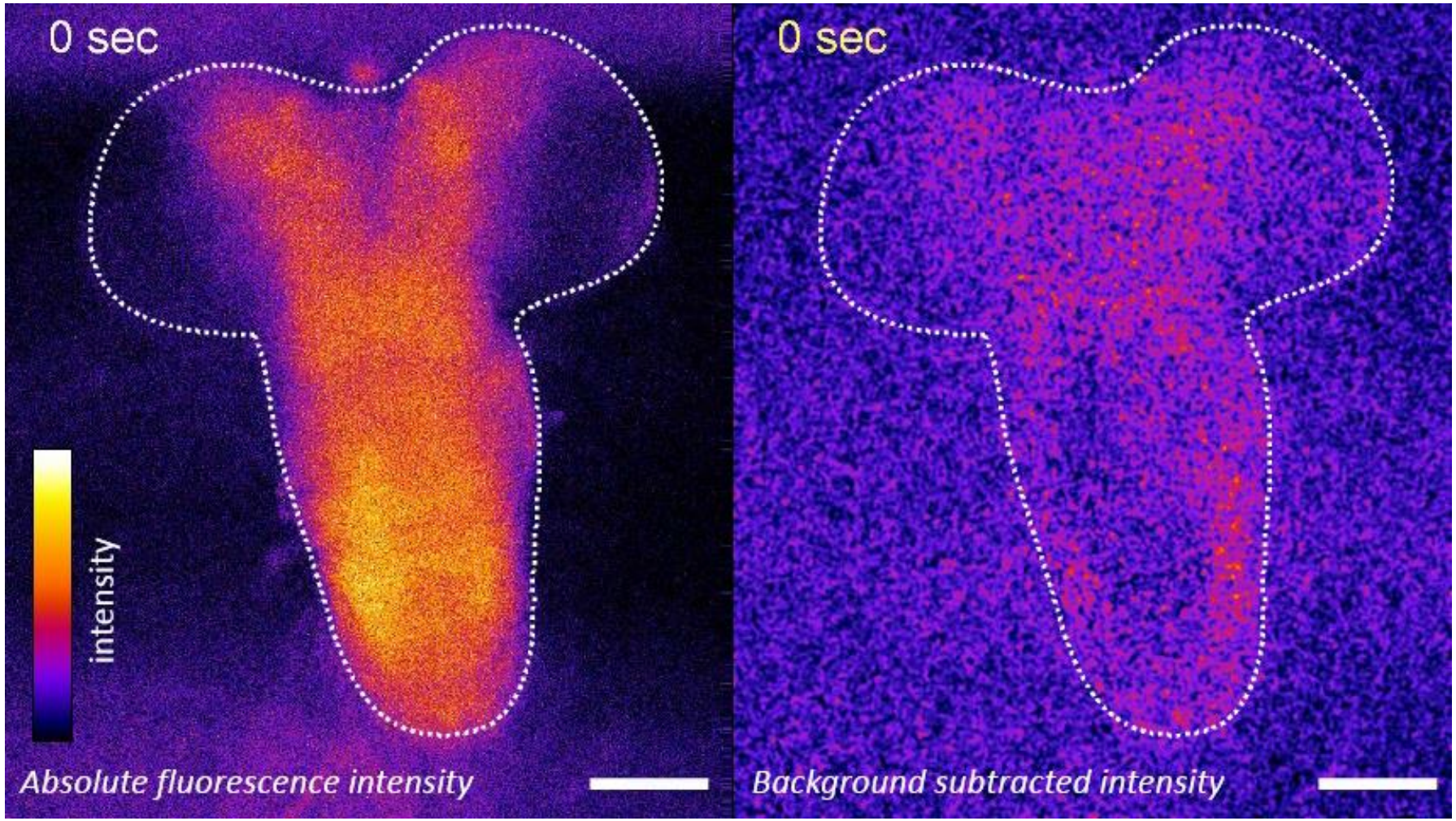




R. Ghaemi *et al.*, *Lab Chip* **15**, 1116 (2015)

C. Murawski et al., *Adv. Mater.* **31**, 1903599 (2019)

Ca-Imaging of Neural Activity with OLEDs

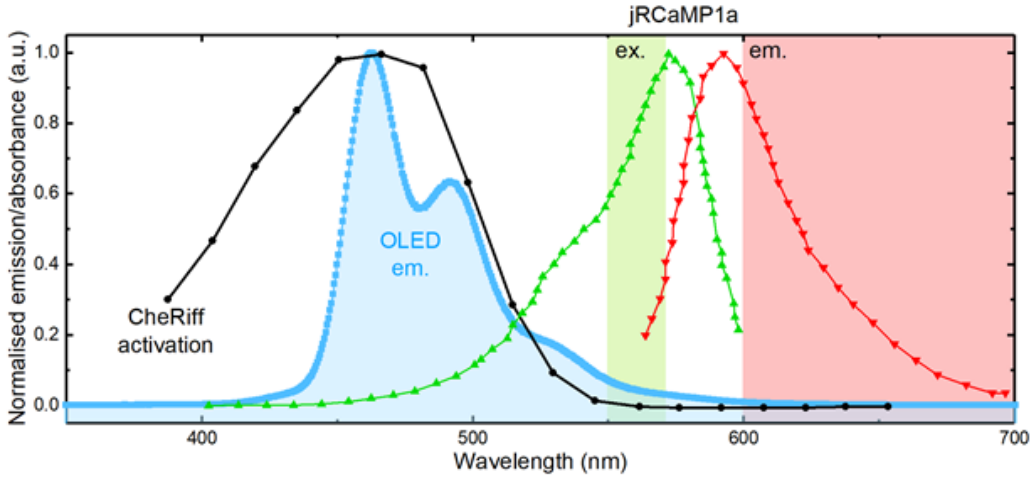


→ *Waveform activity observed resulting from fictive locomotion*

C. Murawski et al., *Adv. Mater.* **31**, 1903599 (2019)

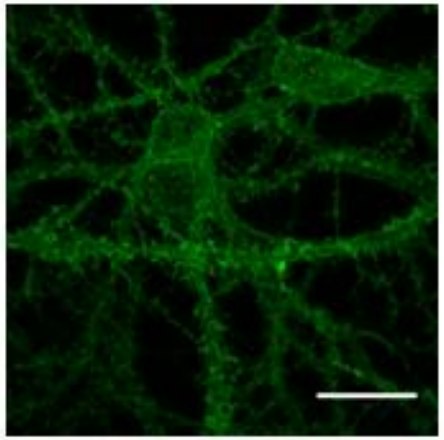
Co-Located Stimulation and Sensing

- Cultured primary mouse hippocampal neurons
- rAAV-transfection with ChR and Ca-indicator → co-located stimulation and sensing



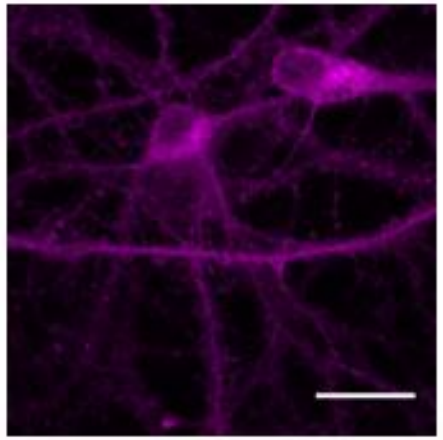
Channelrhodopsin

CheRiff-eGFP

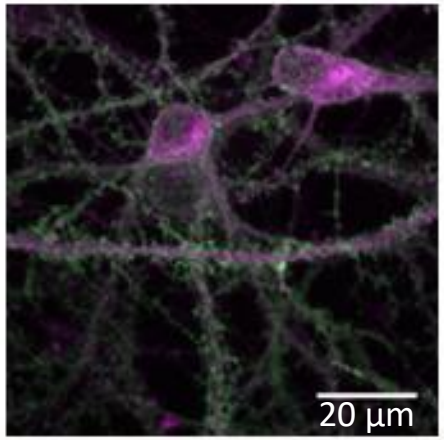


Ca-indicator

jRCaMP1a

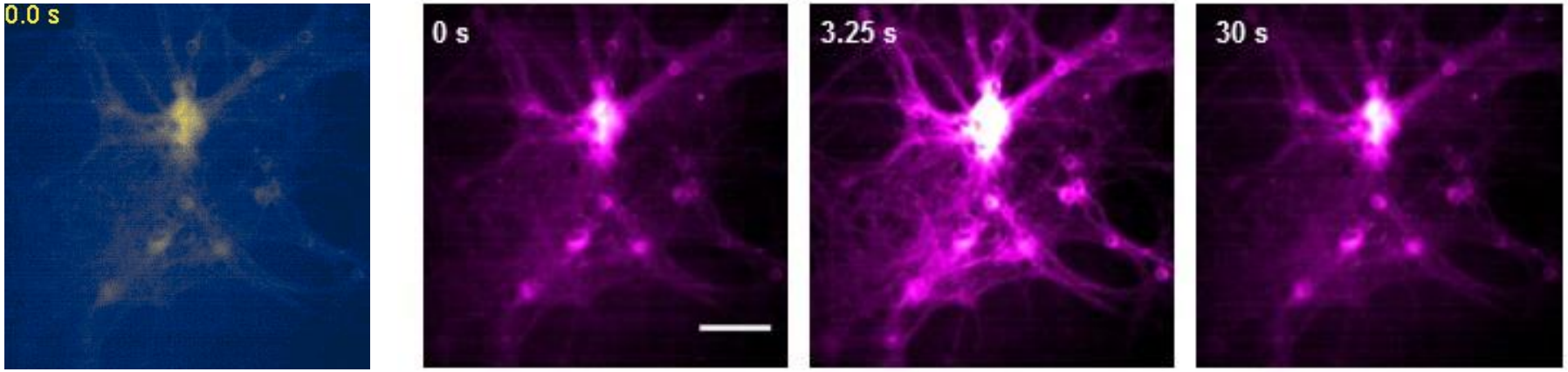


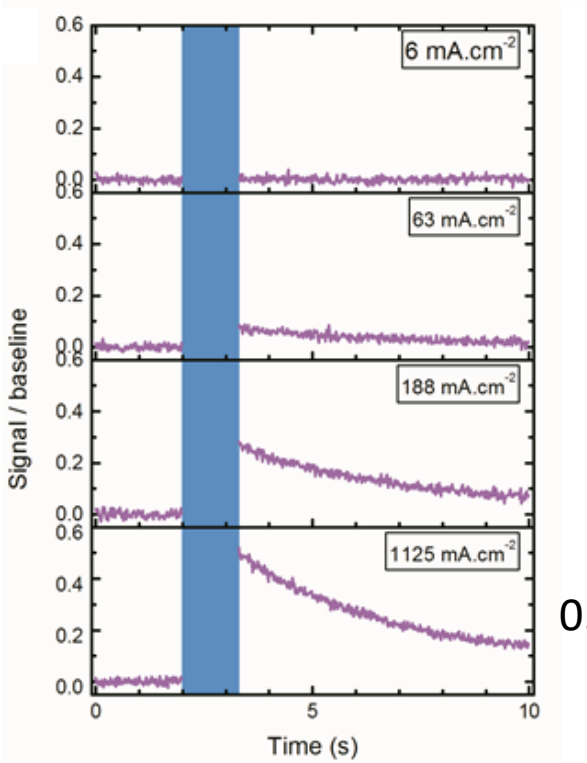
Merged



A. Morton, C. Murawski et al., *Adv. Biosyst.* **3**, 1800290 (2019)

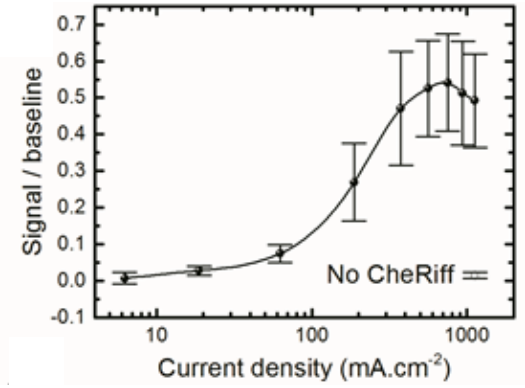
Co-Located Stimulation and Sensing





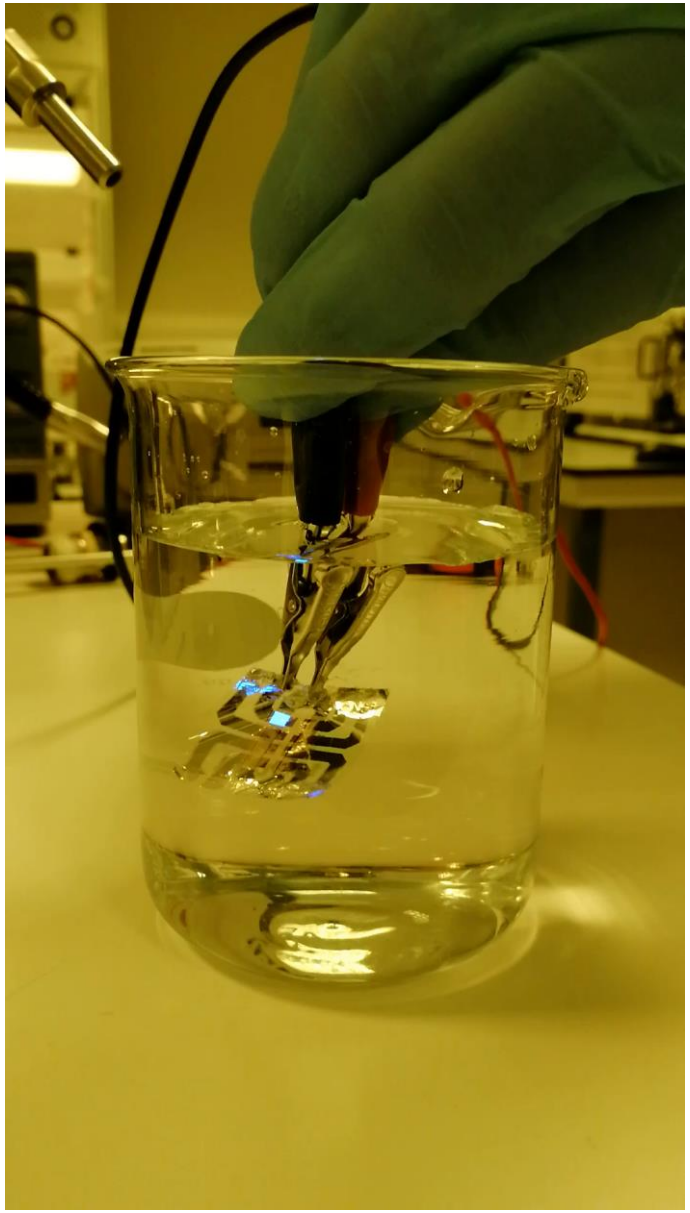
- Intensity-dependent neural activation
- No fluorescence detection during OLED on-time

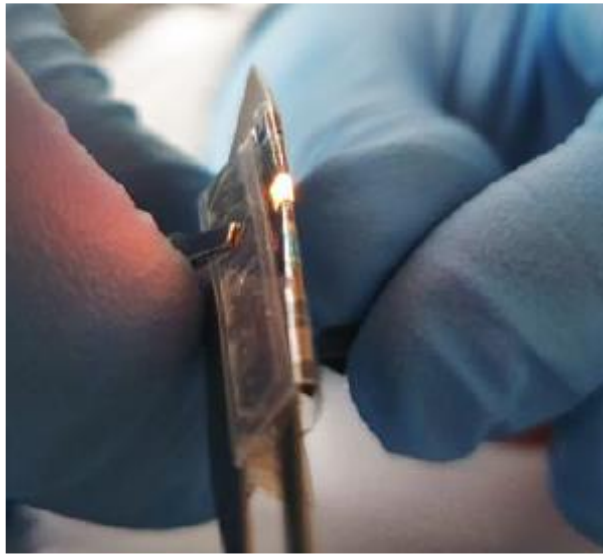
0.8 mW/mm²



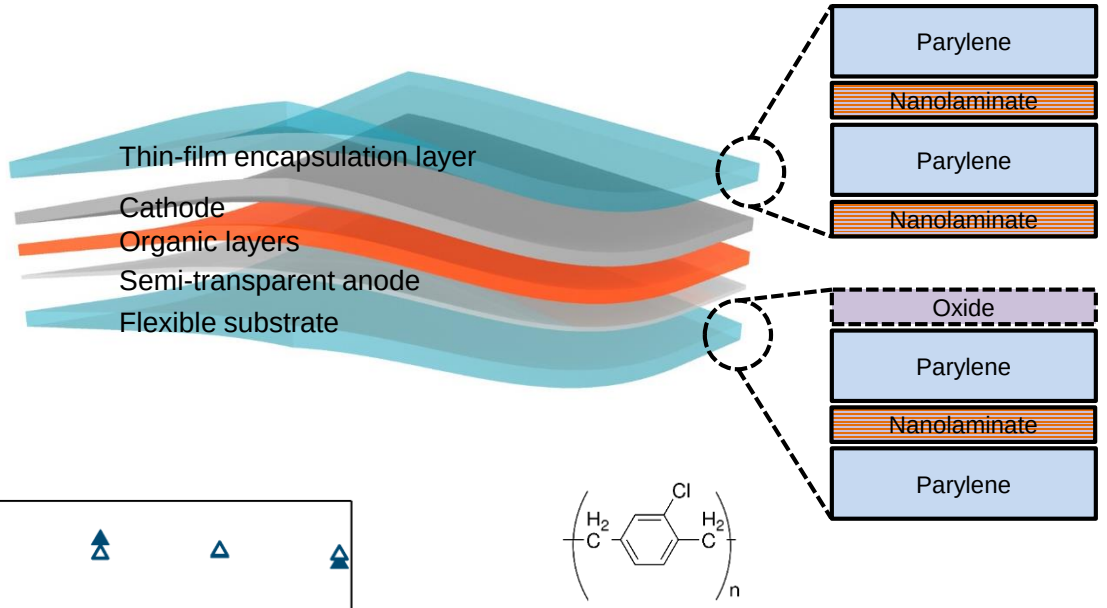
A. Morton, C. Murawski et al., *Adv. Biosyst.* **3**, 1800290 (2019)

Flexible, water-resistant OLEDs

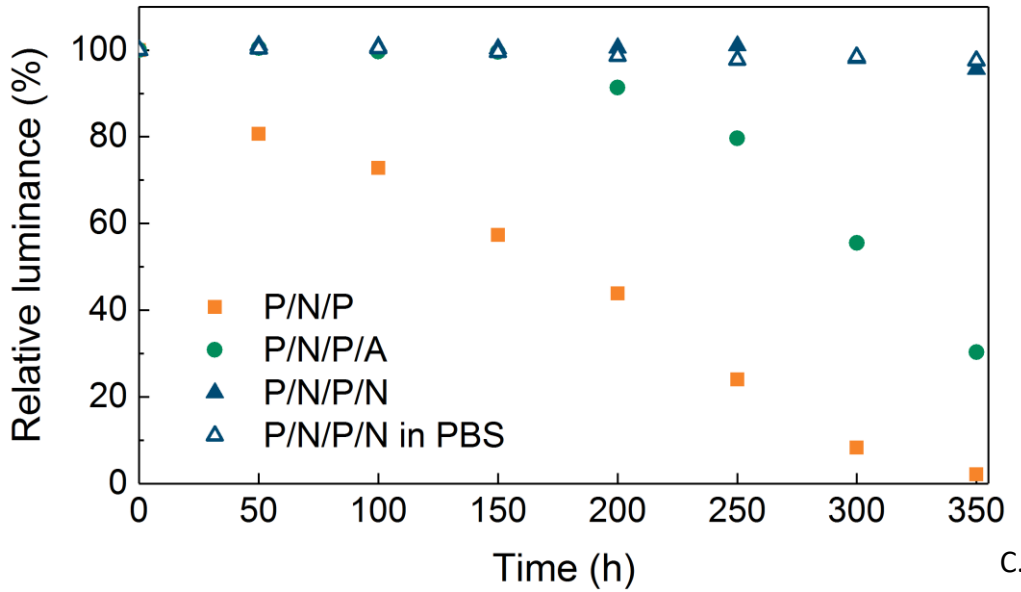




Encapsulation comprising parylene and ALD-processed Al_2O_3/ZrO_2 layers

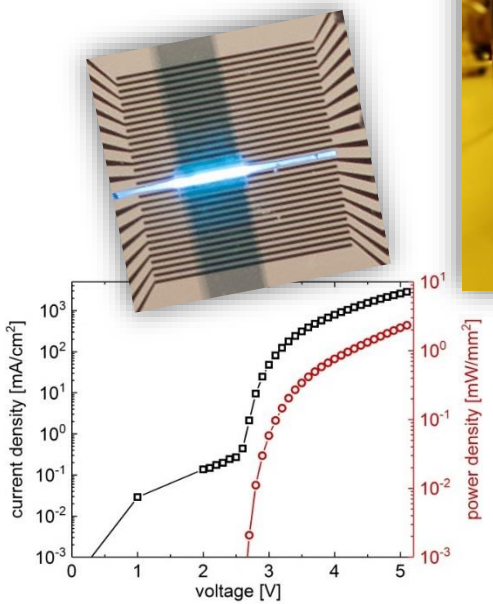


Lifetime in DI water

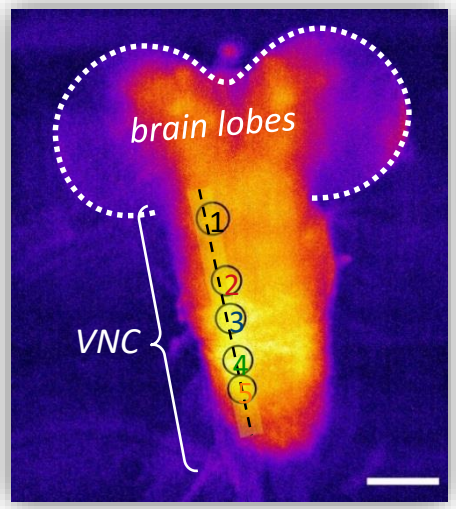


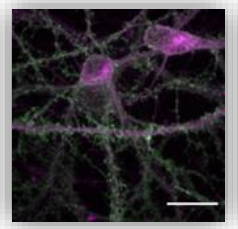
C.-M. Keum, C. Murawski *et al.*, *Nat. Comm.* **11**, 6250 (2020)

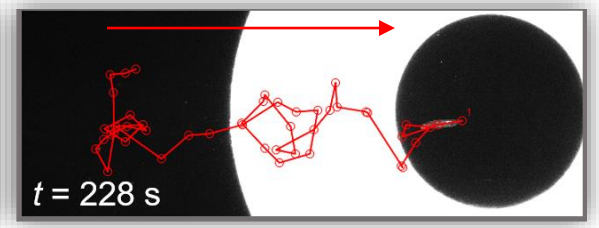
Summary



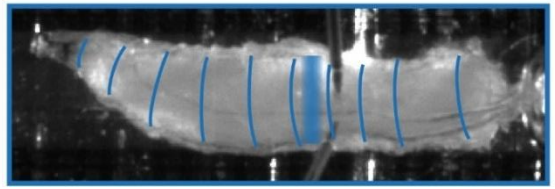
OLED development



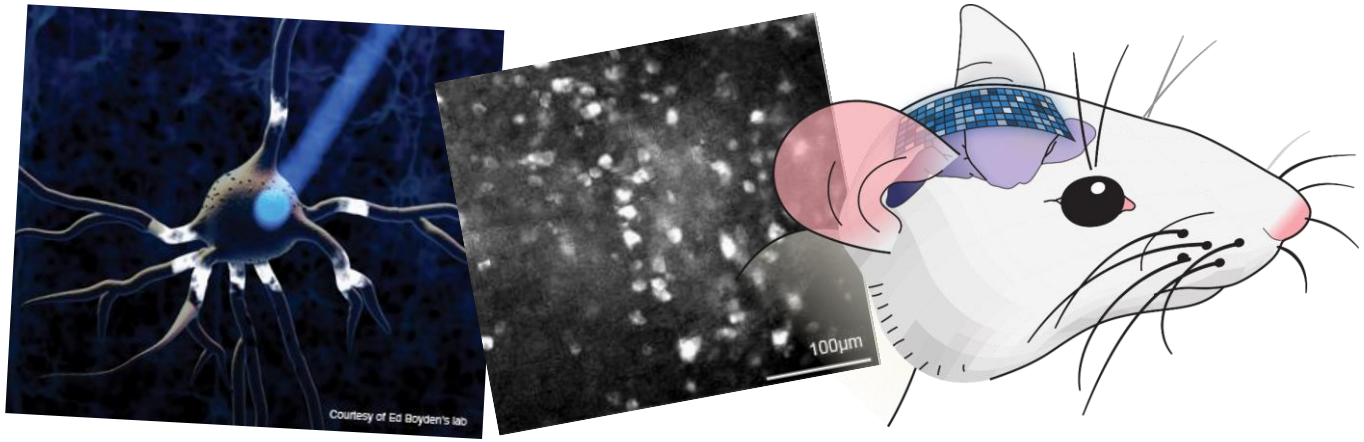




Optogenetic stimulation and sensing



… towards a high-resolution all-optical system for neuronal stimulation and readout!



Acknowledgments

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