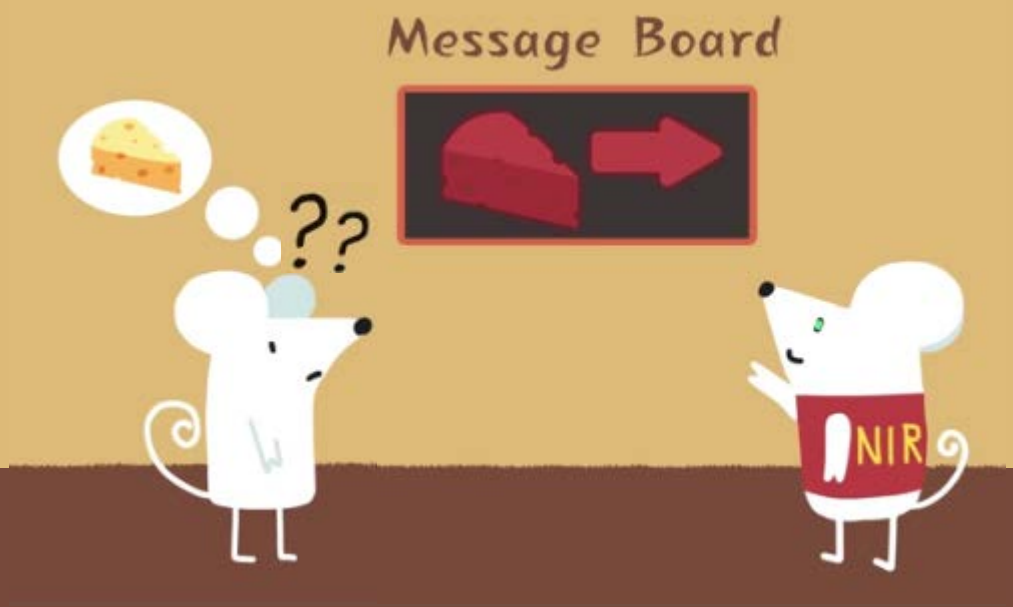
Upconversion Nanoparticles (UCNPs) in Neuroscience



Journal Club, 16th April 2019

Alexandra Bentrup

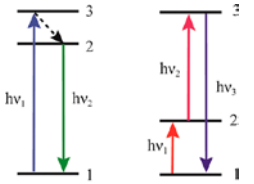
Yuqian Ma *et al.*, *Cell* (2019); https://doi.org/10.1016/j.cell.2019.01.038

Photon upconversion (UC)

CHEMICAL REVIEWS
Review
pubs.acs.org/CR

Upconversion Luminescent Materials: Advances and Applications

Jing Zhou,[†] Qian Liu,[†] Wei Feng, Yun Sun, and Fuyou Li*

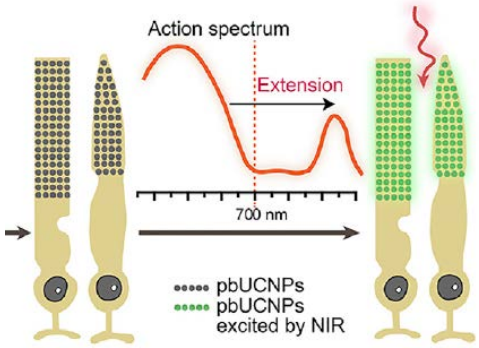


Article

Cell

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

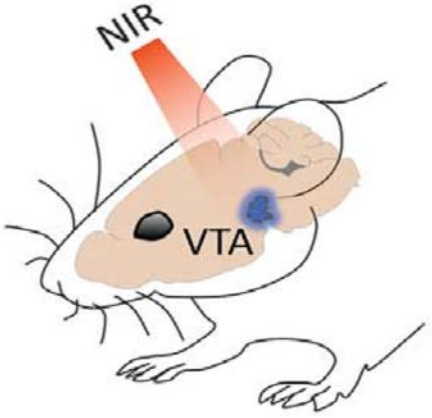
Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]



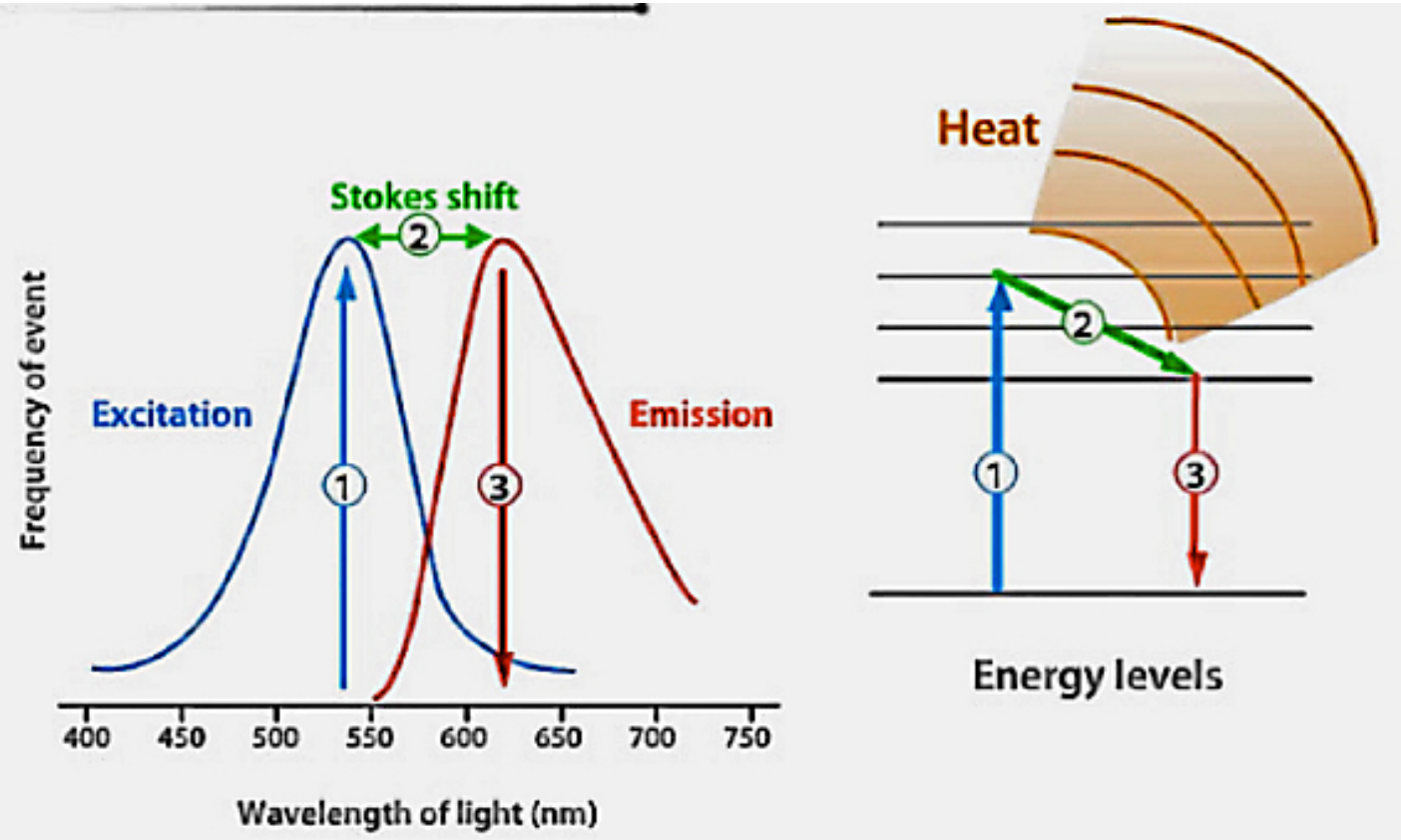
NEUROSCIENCE

Near-infrared deep brain stimulation via upconversion nanoparticle–mediated optogenetics

Shuo Chen,[1*] Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9*] Thomas J. McHugh[1,10*]

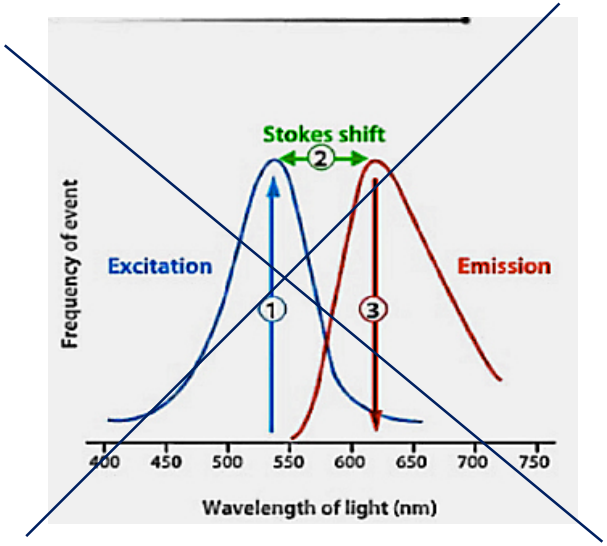


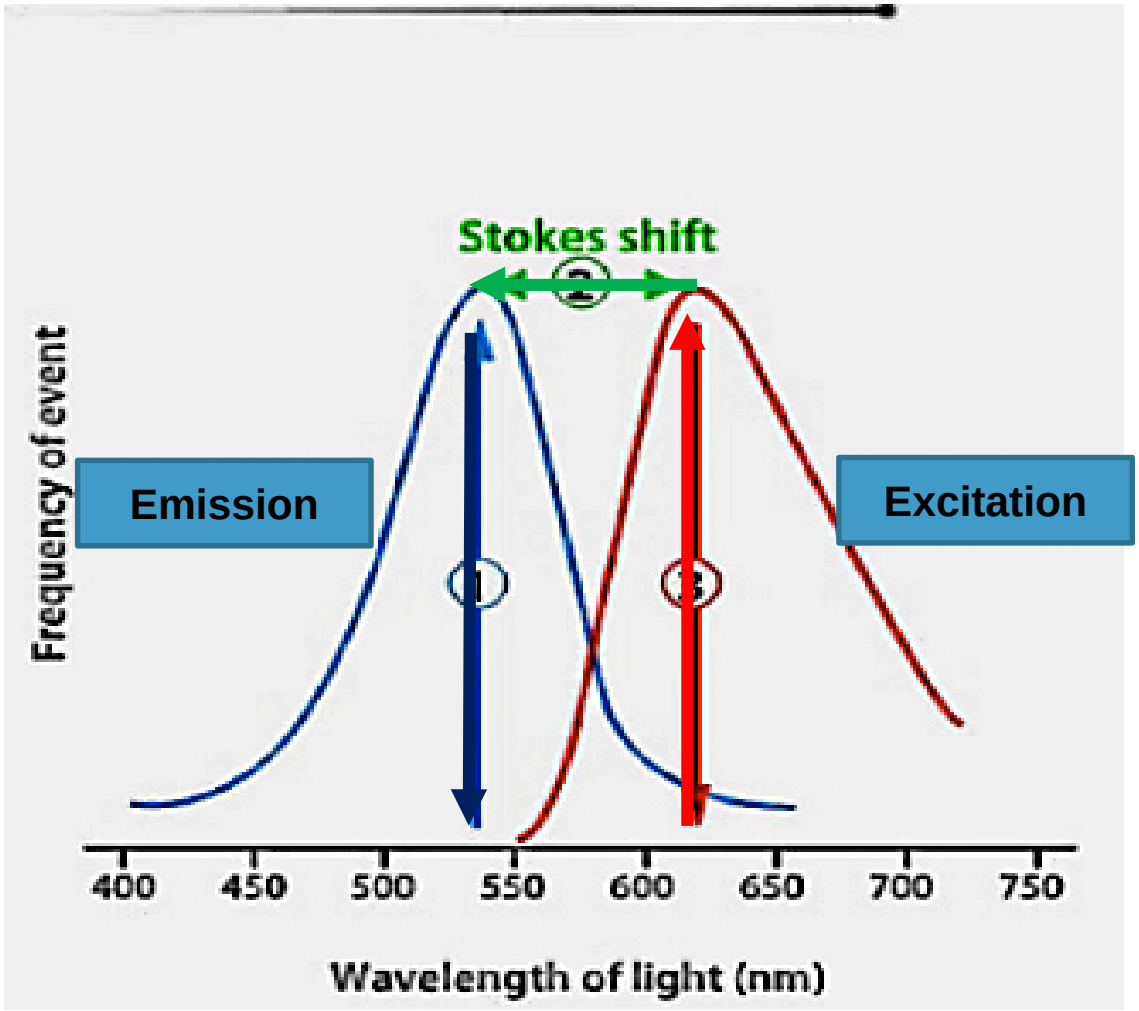
Traditional downconversion: Fluorescent dyes



https://www.thermofisher.com/ch/en/home/life-science/cell-analysis/cell-analysis-learning-center/molecular-probes-school-of-fluorescence/fluorescence-basics/anatomy-fluorescence-spectra/jcr:content/MainParsys/textimage_b040/image.img.320.medium.jpg/1498935287060.jpg

Photon upconversion (UC)



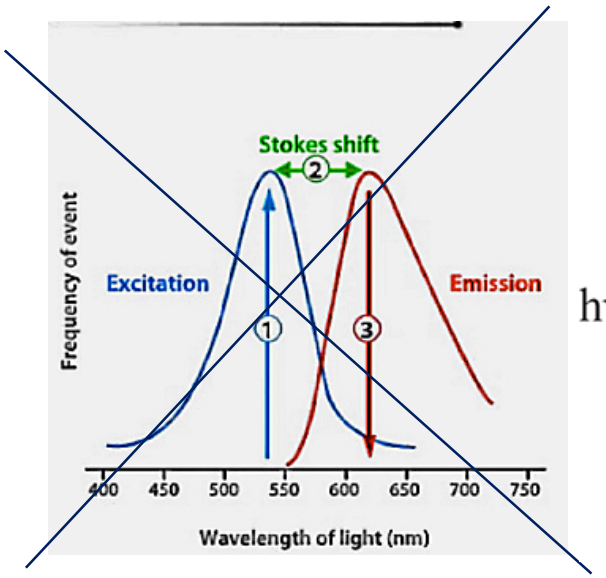


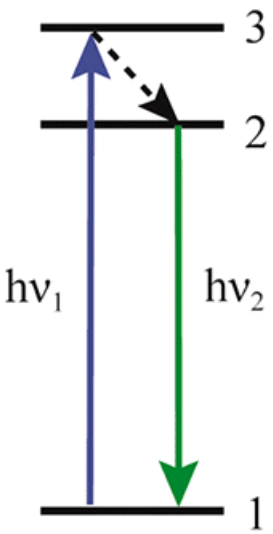
https://www.thermofisher.com/ch/en/home/life-science/cell-analysis/cell-analysis-learning-center/molecular-probes-school-of-fluorescence/fluorescence-basics/anatomy-fluorescence-spectra/jcr:content/MainParsys/textimage_b040/image.img.320.medium.jpg/1498935287060.jpg

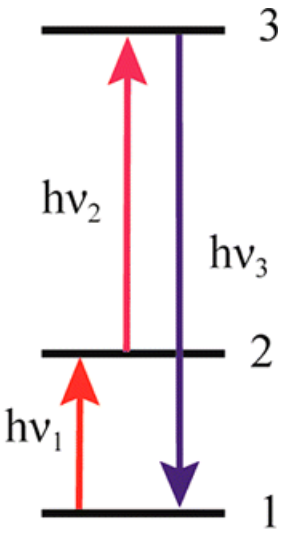
Jing Zhou, 2015 Chem. Rev.

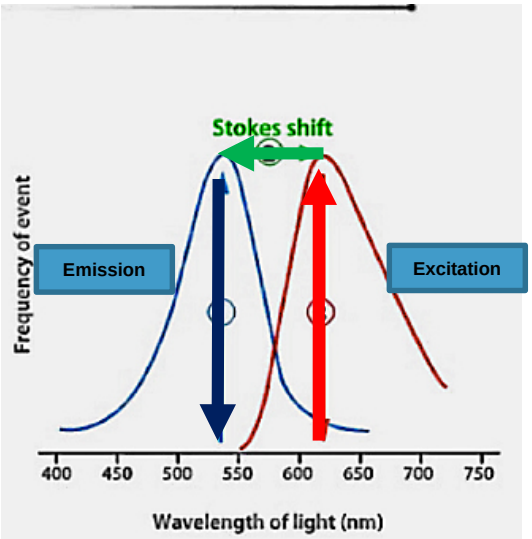
Photon upconversion (UC)

- sequential absorption of ≥2 photons
  → emission of light at **shorter** wavelength than the excitation wavelength
- anti-Stokes type emission
- E.g infrared light to visible light







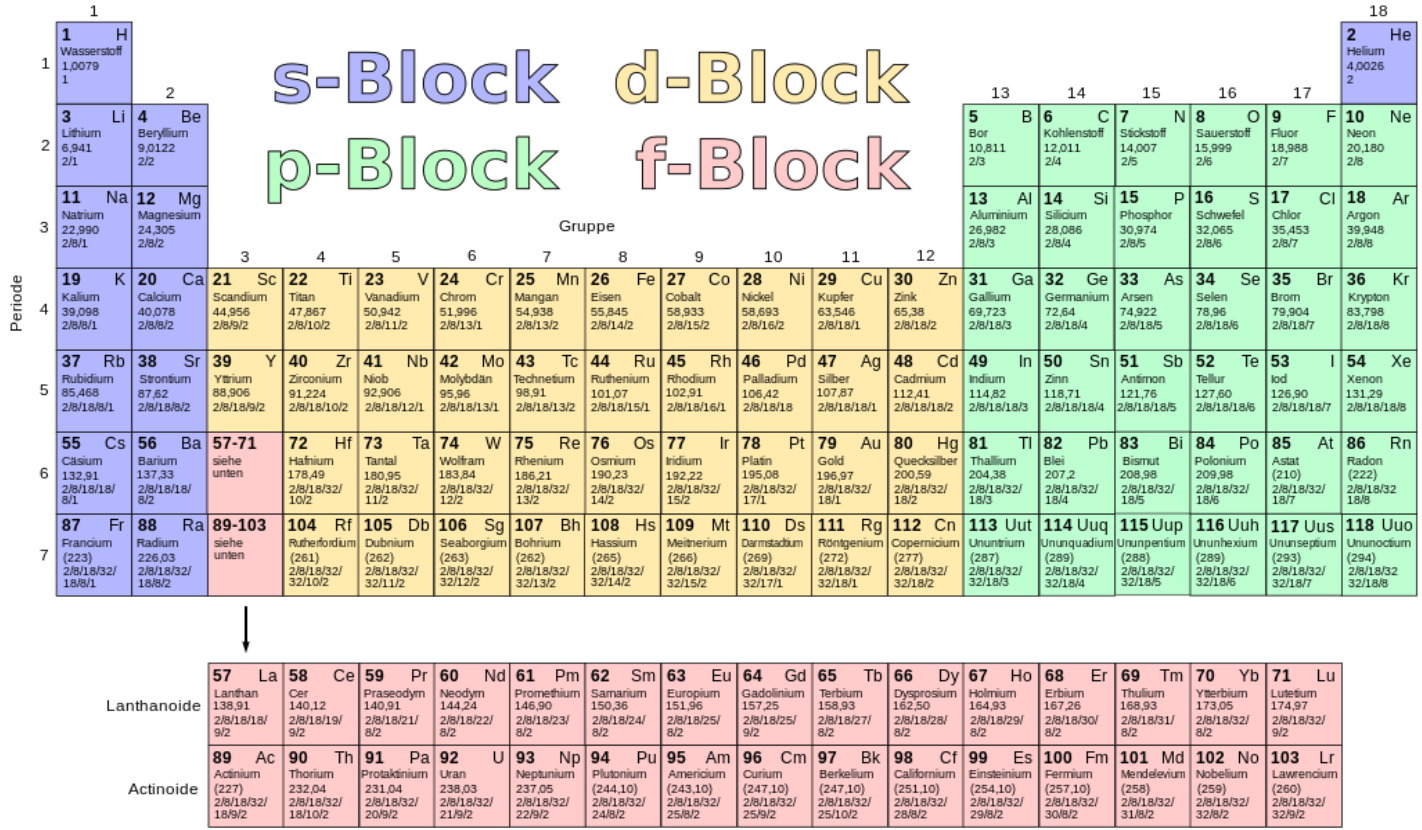


https://www.thermofisher.com/ch/en/home/life-science/cell-analysis/cell-analysis-learning-center/molecular-probes-school-of-fluorescence/fluorescence-basics/anatomy-fluorescence-spectra/jcr:content/MainParsys/textimage_b040/image.img.320.medium.jpg/1498935287060.jpg

Jing Zhou, 2015 Chem. Rev.

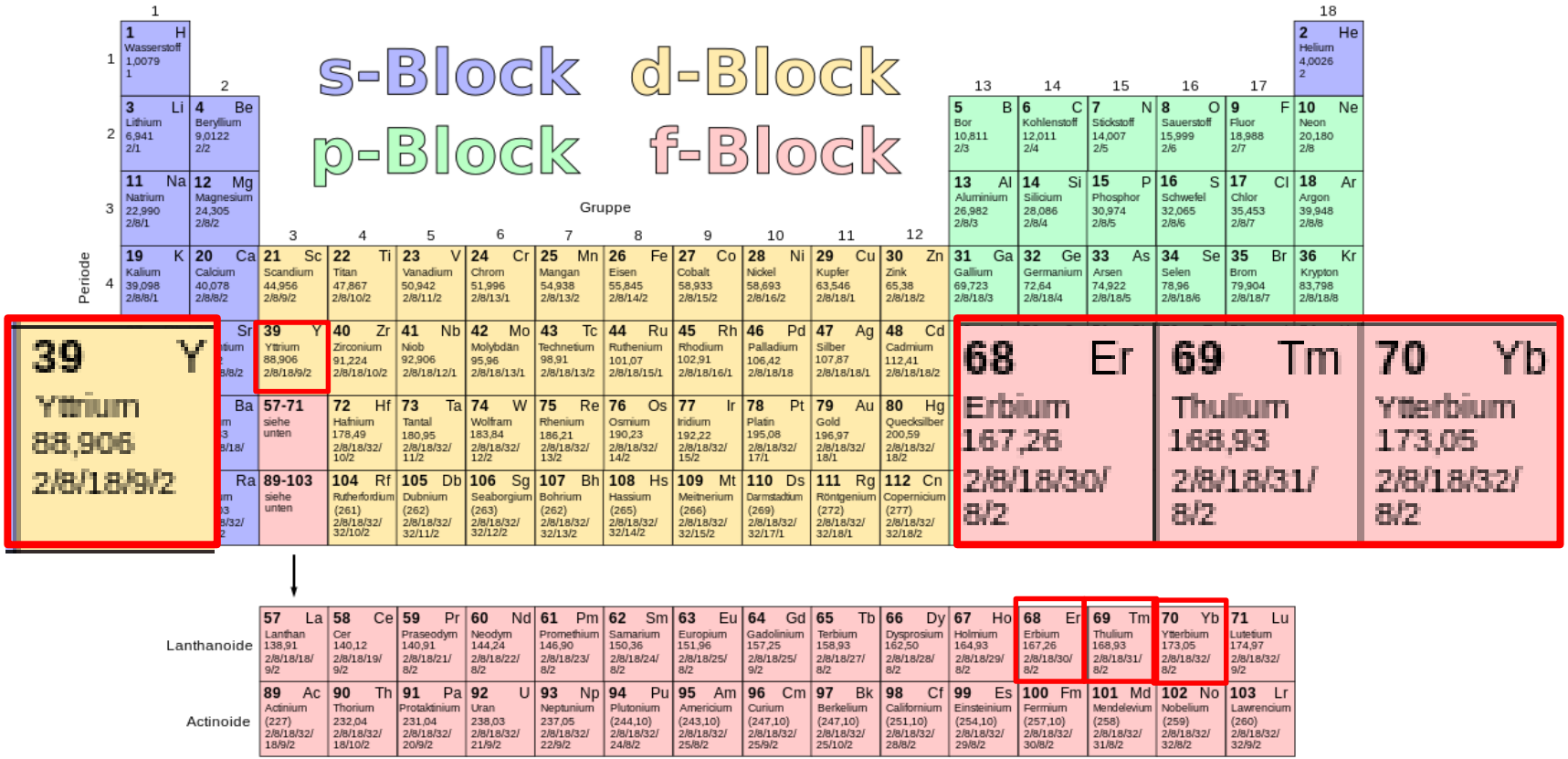
Photon upconversion (UC)

- Organic (polycyclicaromatic hydrocarbons)
- Inorganic: often contain ions of d-block or f-block elements



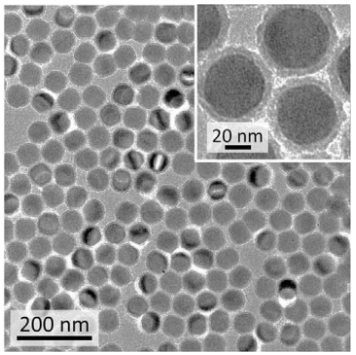
Photon upconversion (UC)

- Organic (polycyclicaromatic hydrocarbons)
- **Inorganic**: often contain ions of d-block or f-block elements



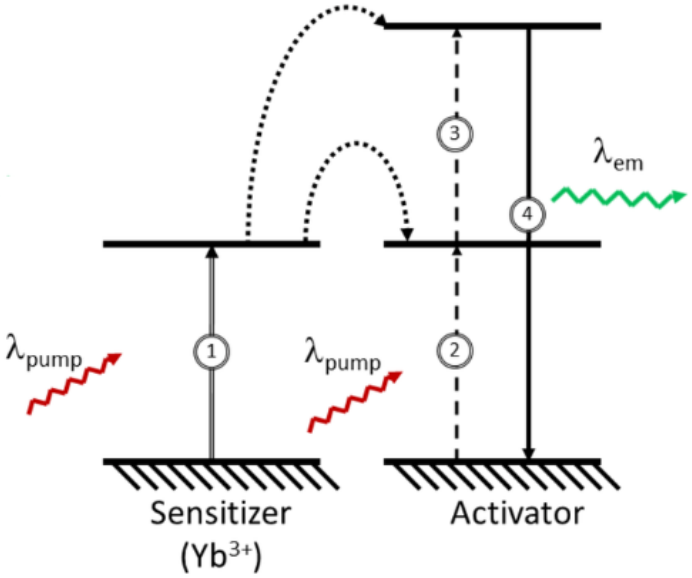
Photon upconversion (UC)

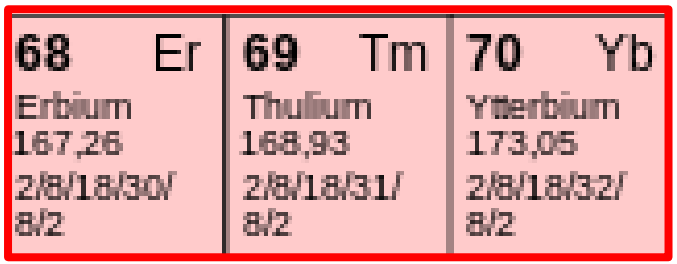
- Inorganic:
  - NaYF4 = popular host for lanthanide UCNPs
    Sodium yttrium fluoride (1:1:4)
  - Dopant ions Er3+, Tm3+ = activators (<2 mol %)
  - Yb3+ is often codoped as a sensitizer to enhance upconversion emission Jing Zhou, 2015 Chem. Rev.



Shuo Chen, 2018, Science

Host





Activators Sensitizer

https://upload.wikimedia.org/wikipedia/commons/thumb/a/a7/Orbitalb
l%C3%B6cke.svg/1024px-Orbitalbl%C3%B6cke.svg.png?155378776362 3

Rafik Naccache 2012, Cancers, https://doi.org/10.3390/cancers4041067

Photon upconversion (UC)

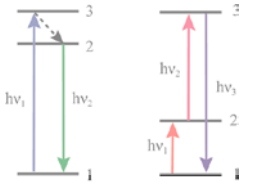
CHEMICAL REVIEWS

Review

pubs.acs.org/CR

Upconversion Luminescent Materials: Advances and Applications

Jing Zhou,† Qian Liu,† Wei Feng, Yun Sun, and Fuyou Li*

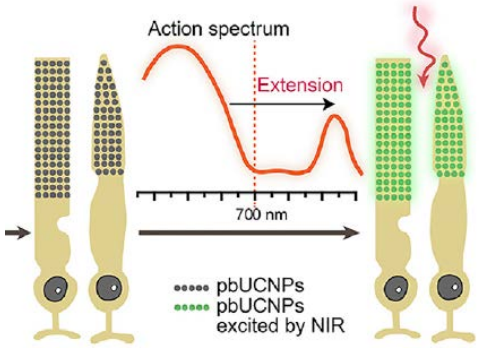


Article

Cell

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]



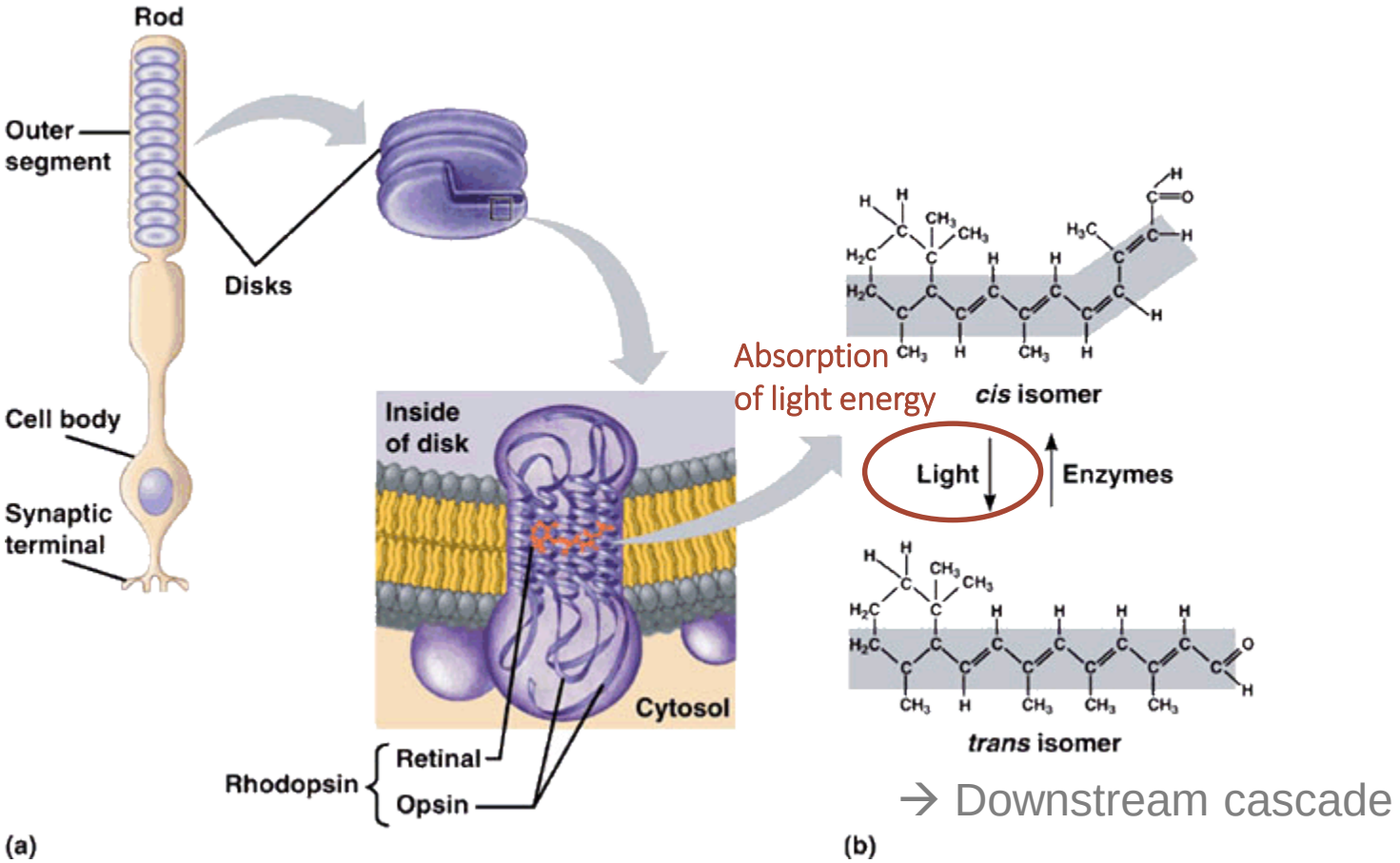
NEUROSCIENCE

Near-infrared deep brain stimulation via upconversion nanoparticle–mediated optogenetics

Shuo Chen,[1*] Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9*] Thomas J. McHugh[1,10*]

Near-Infrared Vision

- Opsins would have to be very sensitive to low energy



→ Downstream cascade

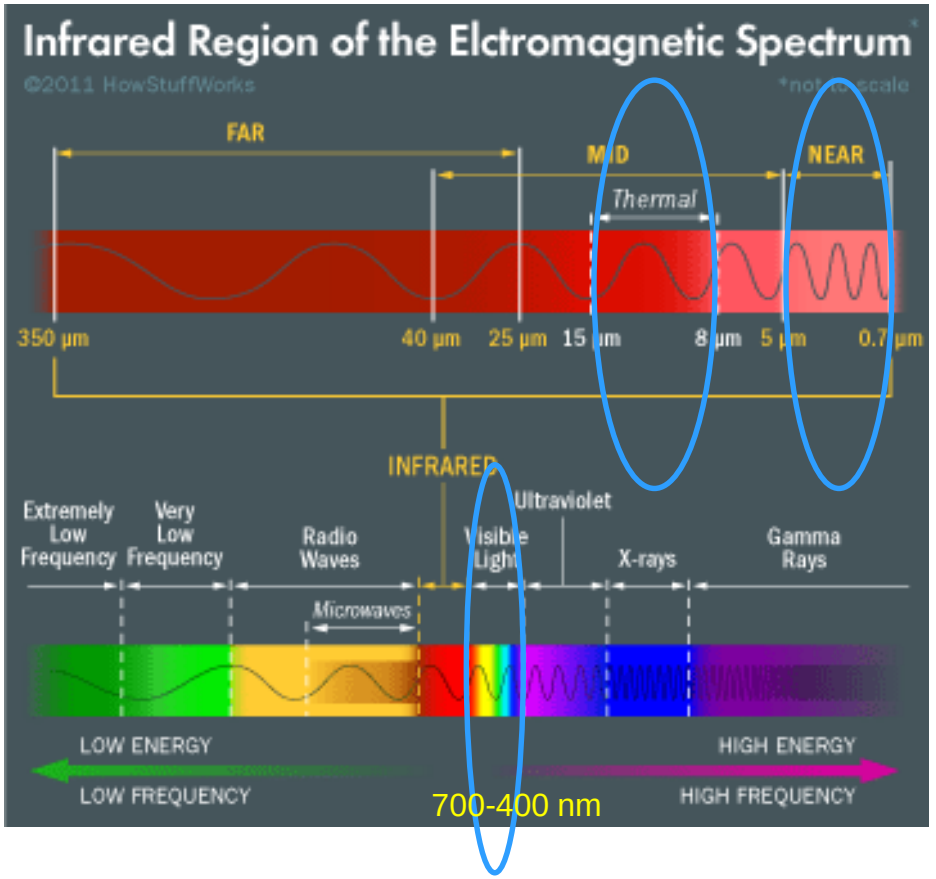
http://www.chm.bris.ac.uk/motm/retinal/retinalh.htm

Near-Infrared Vision

- Opsins would have to be very sensitive to low energy → thermal noise

→ Dong-Gen Luo, 2011 Science

- Alternative: Conversion to higher energy signal via **photoreceptor-binding upconversion nanoparticles (pbUCNPs)**

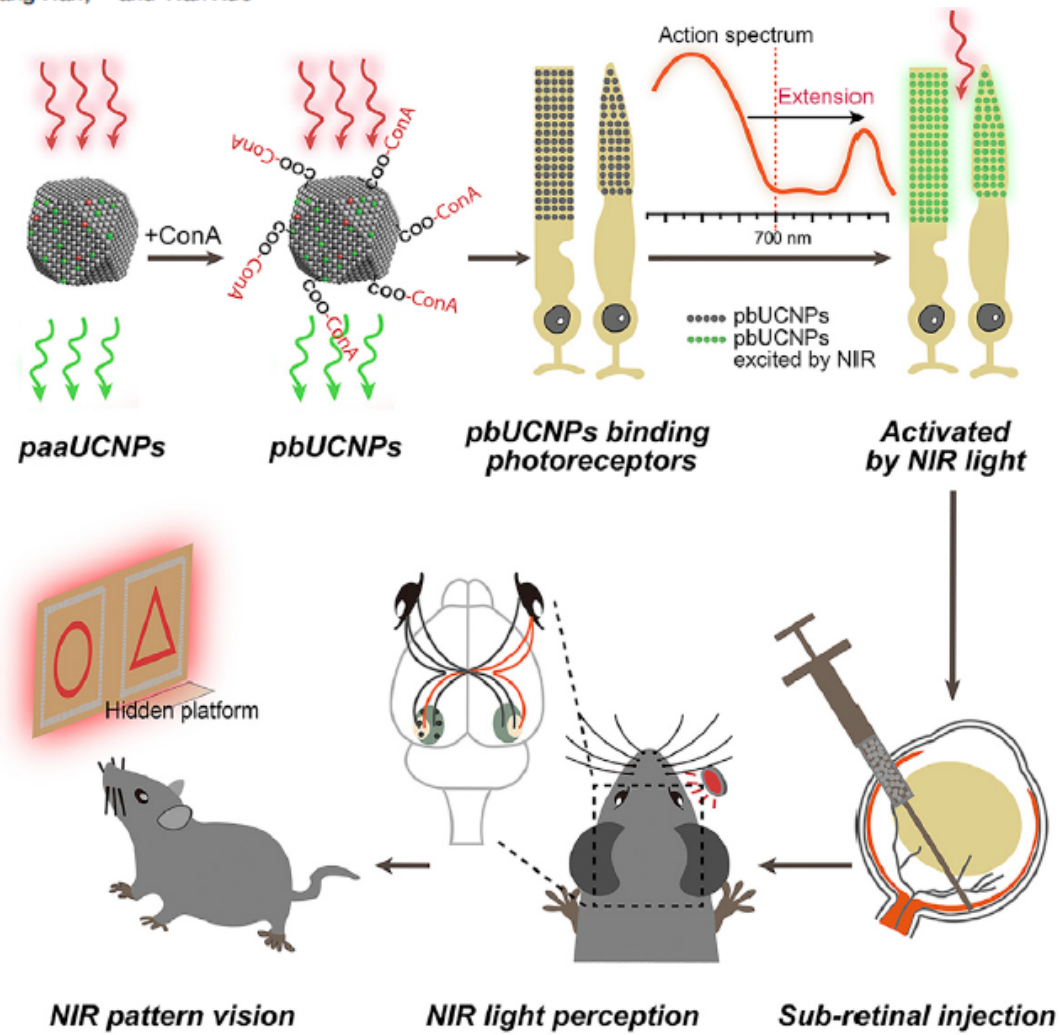


https://www.autodesk.com/products/eagle/blog/electromagnetic-wireless-electronic-basics/

Cell

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]



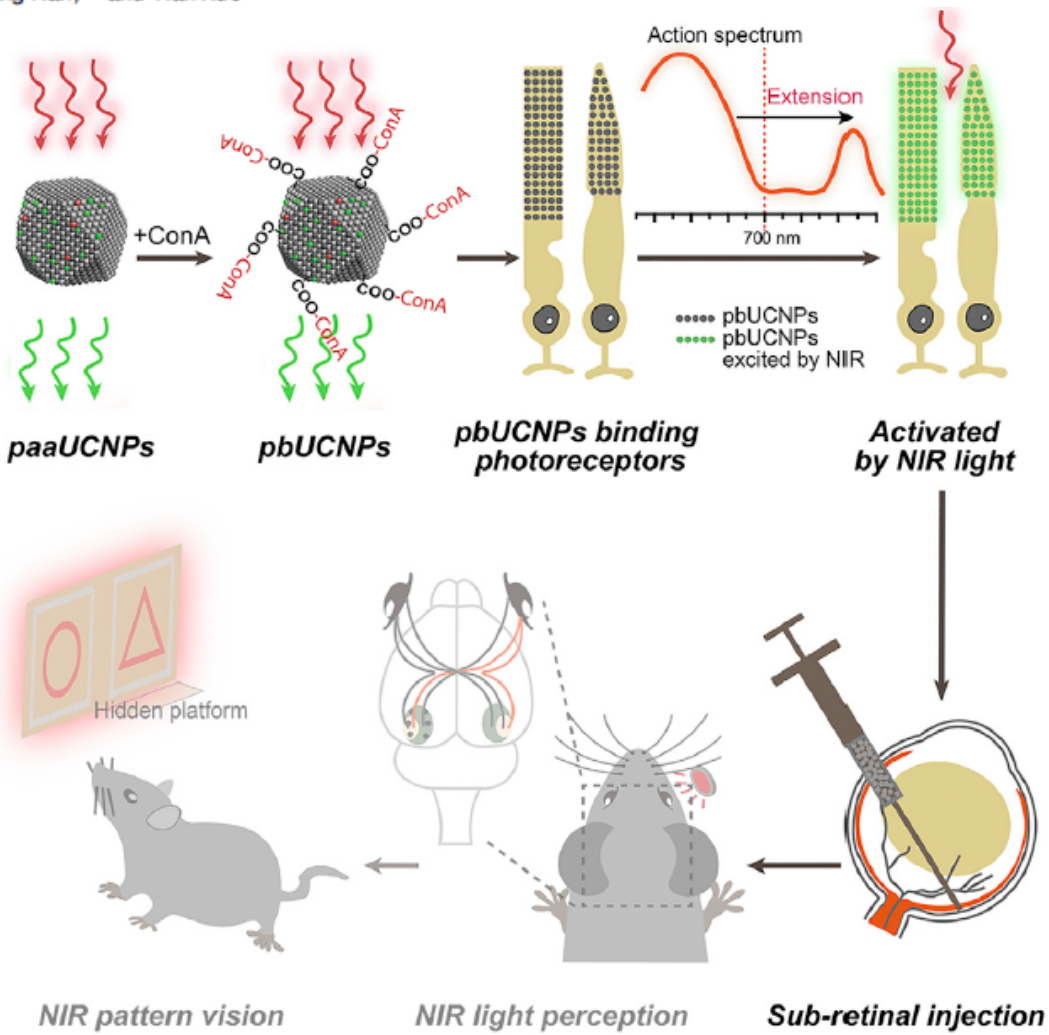
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

- Self-powered
- Biocompatible
- Injectable

Cell

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

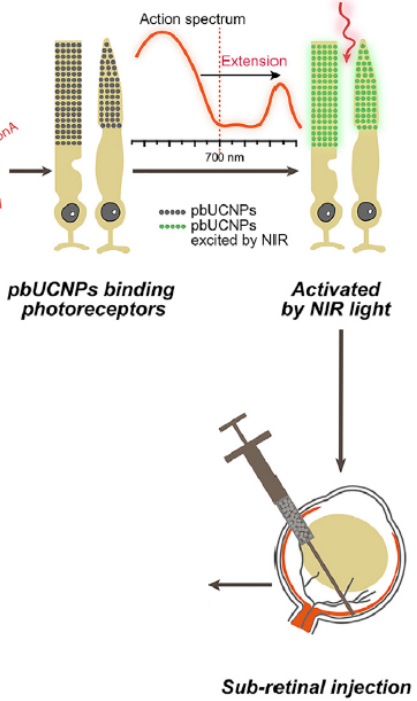
Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]



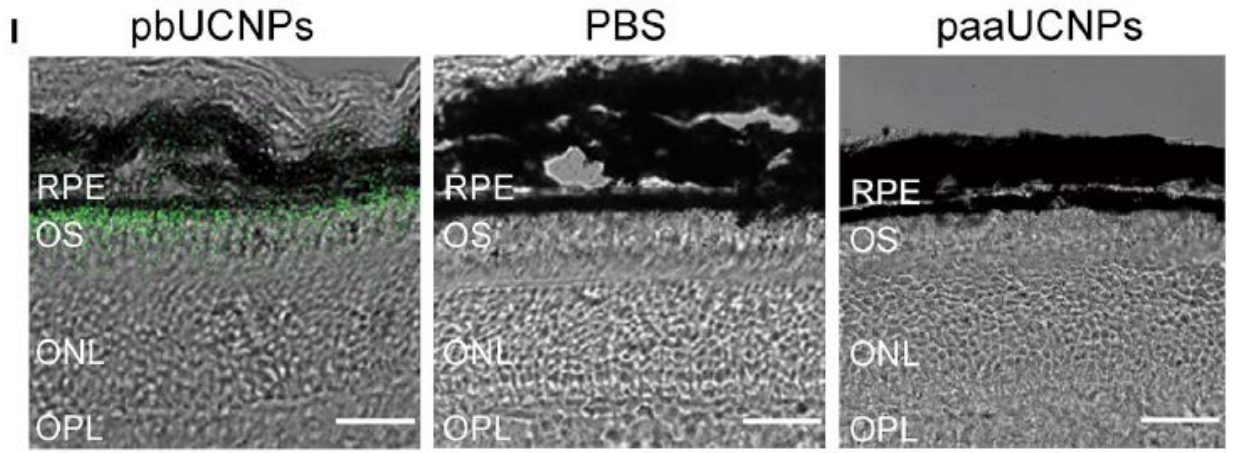
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

- Self-powered
- Biocompatible
- Injectable

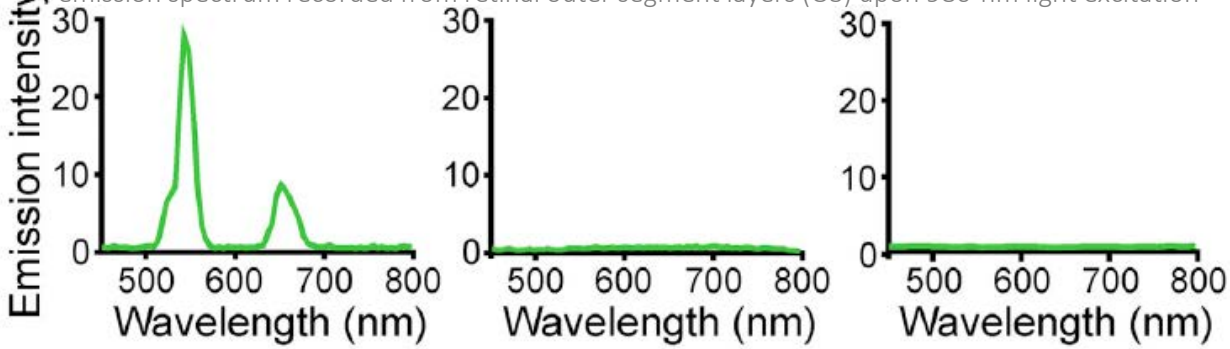
poly acrylic acid coated UCNPs (paaUCNP)
+ concanavalin A protein (ConA)
→ glycosidic bonds with
sugar residues on OS of photo receptors



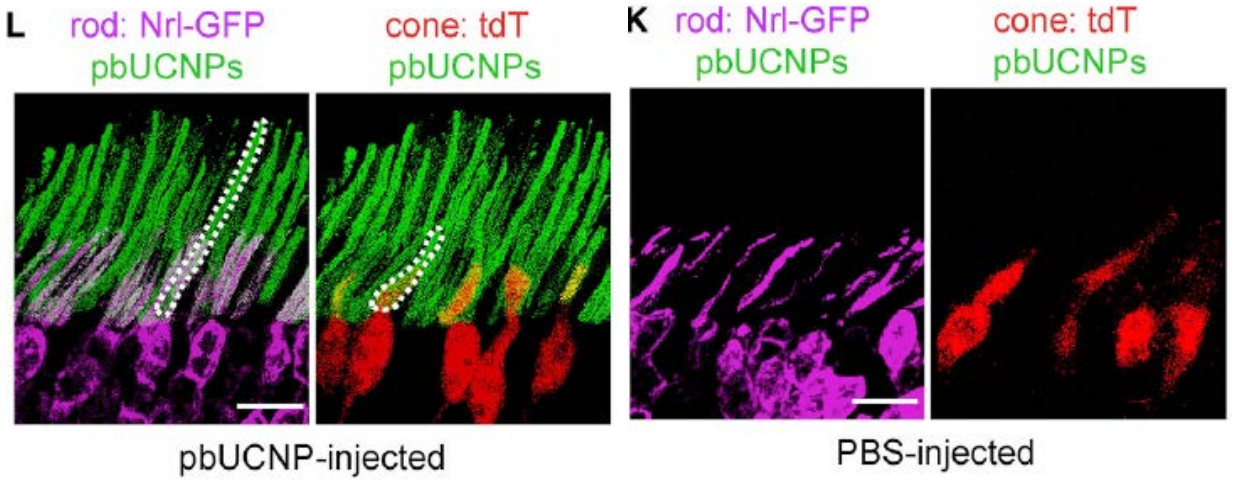
overlays of transmission and luminescence optical images (green: 980-nm ex/535-nm em) of retinal slices



emission spectrum recorded from retinal outer segment layers (OS) upon 980-nm light excitation



continuous inner
and outer segments



Article

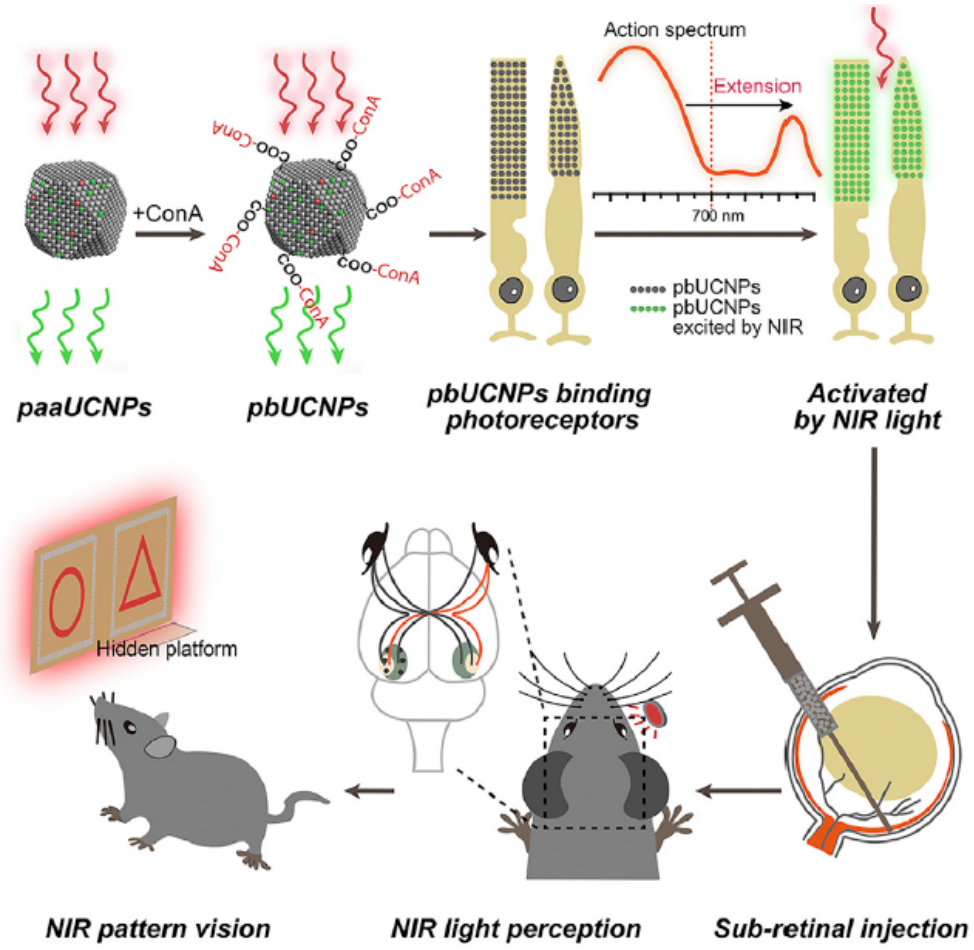
Cell

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]

photoreceptor-binding upconversion nanoparticles (pbUCNPs)

- Self-powered
- **Biocompatible**
- Injectable

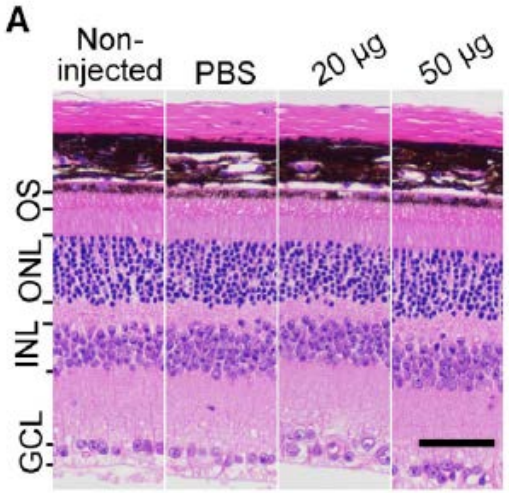


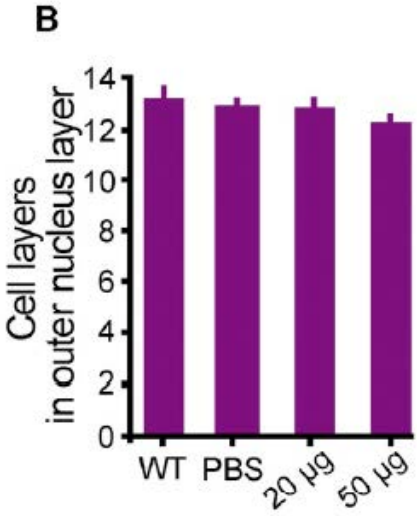
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

- Self-powered
- Biocompatible
- Injectable

Side effects e.g. cataracts, corneal opacity
Only minor, transient (2 weeks)
Comparable to any sub-retinal injection

X retinal degeneration
X inflammation (Iba1 stain)
X apoptosis (TUNEL stain)



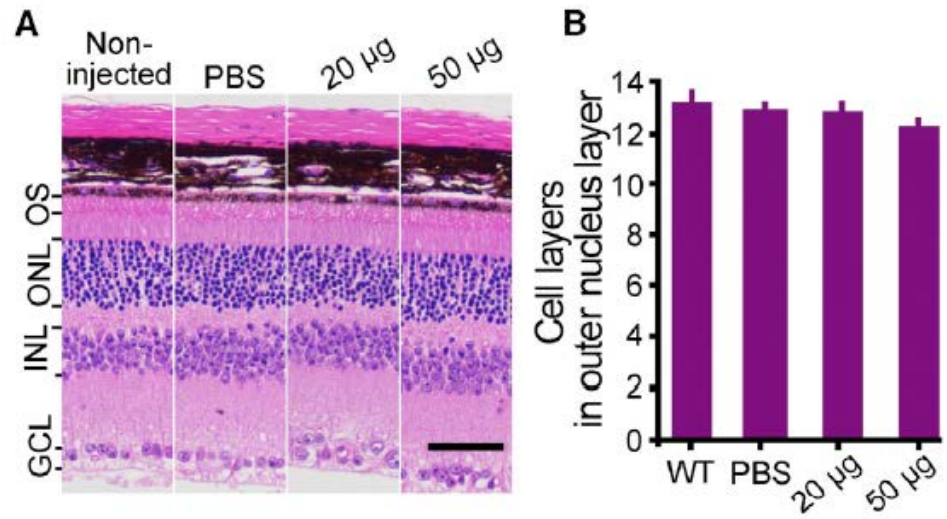


photoreceptor-binding upconversion nanoparticles (pbUCNPs)

- Self-powered
- Biocompatible
- Injectable

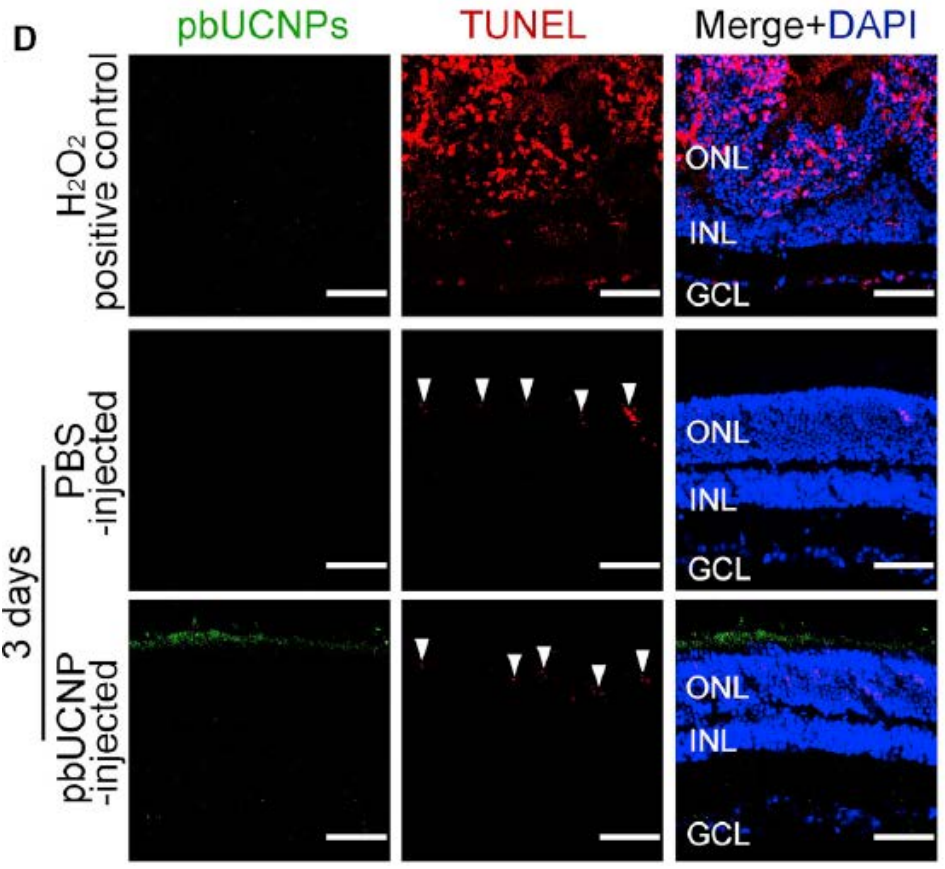
Side effects e.g. cataracts, corneal opacity
Only minor, transient (2 weeks)
Comparable to any sub-retinal injection

X retinal degeneration
X inflammation (Iba1 stain)
X apoptosis (TUNEL stain)



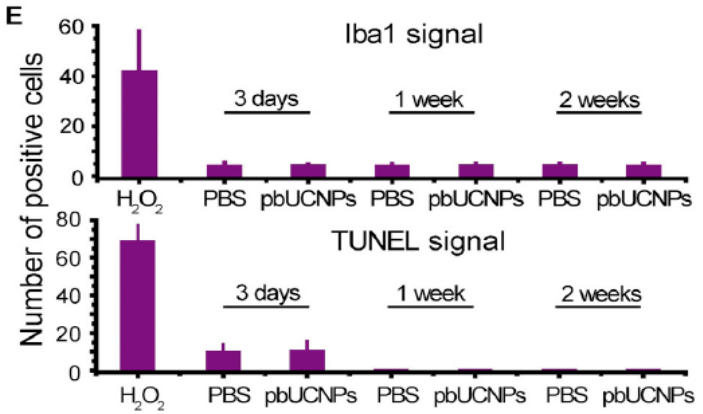
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

- Self-powered
- **Biocompatible**
- Injectable



Side effects e.g. cataracts, corneal opacity
Only minor, transient (2 weeks)
Comparable to any sub-retinal injection

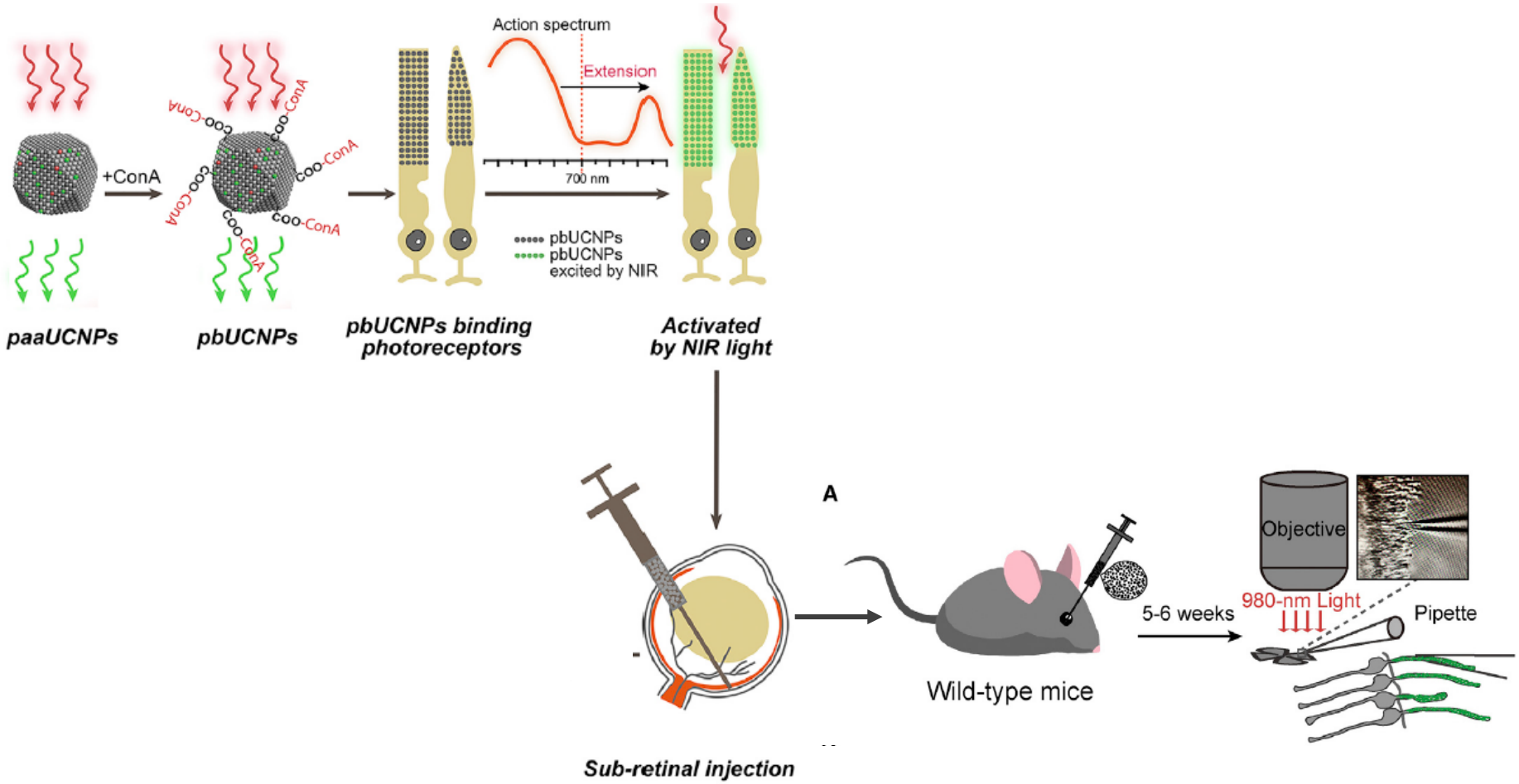
X retinal degeneration
X **inflammation** **(Iba1 stain)**
X **apoptosis** **(TUNEL stain)**



photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Photoreceptor Activation**:

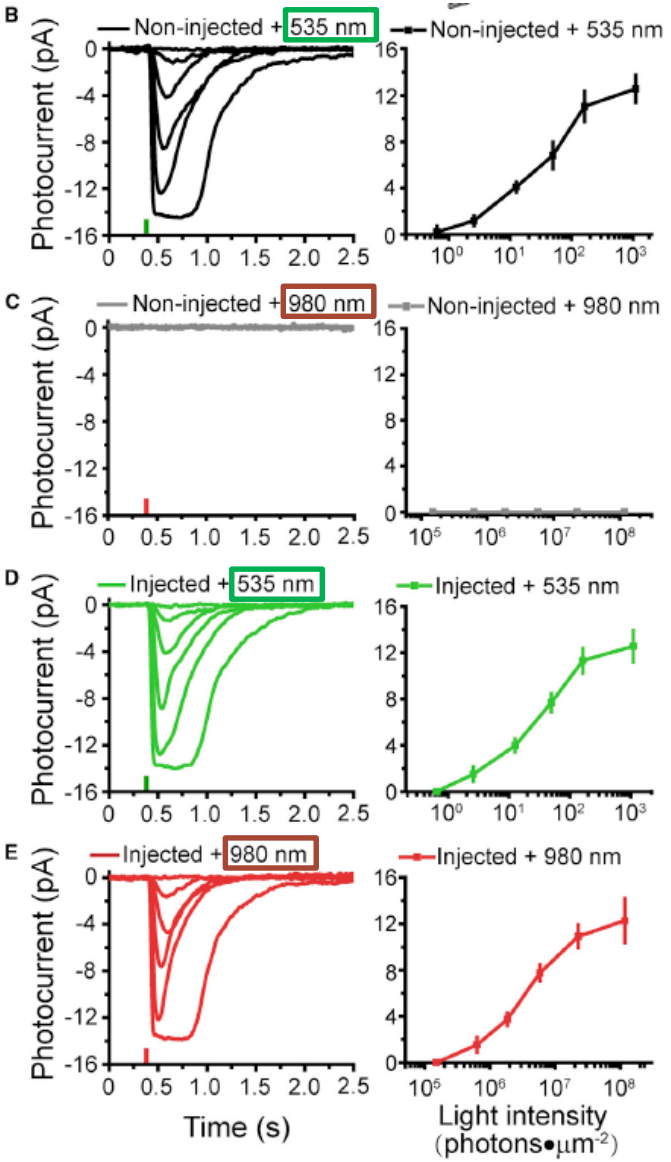
- Single rod pipette recordings on acutely dissected retinae
- Population response *in vivo* in ERG



photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Photoreceptor Activation**:

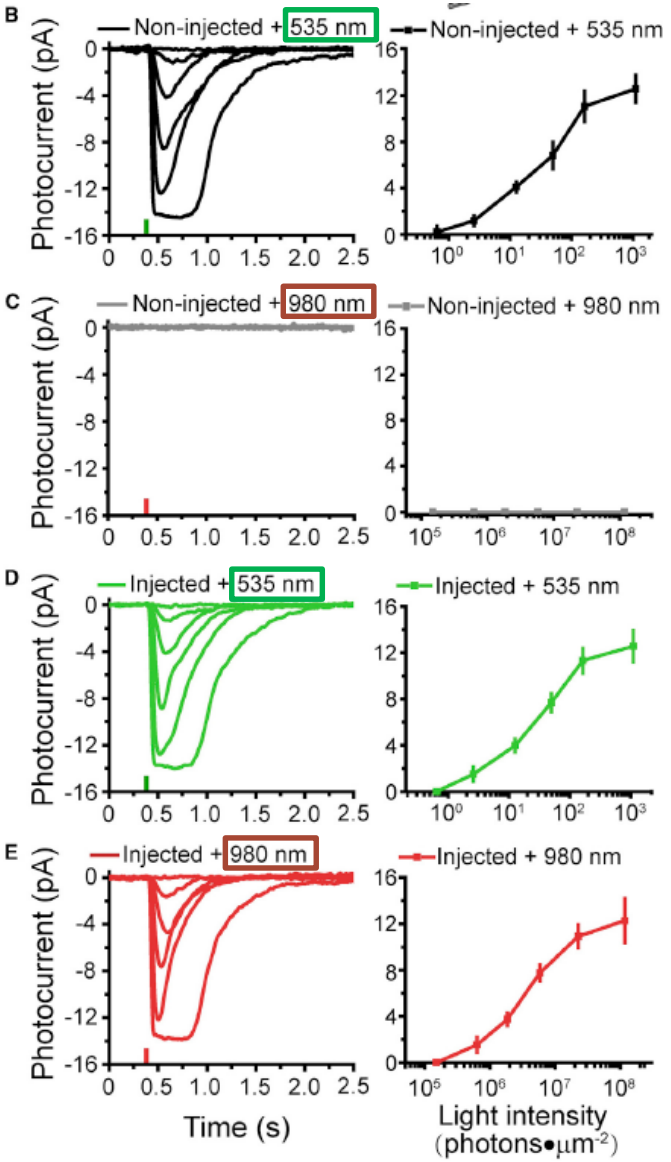
- Single rod pipette recordings on acutely dissected retinae
  - Amplitude and kinetics of photocurrents elicted by NIR vs VL were identical
  - No delay in response to NIR compared to VL
  - No alteration of light adaptation



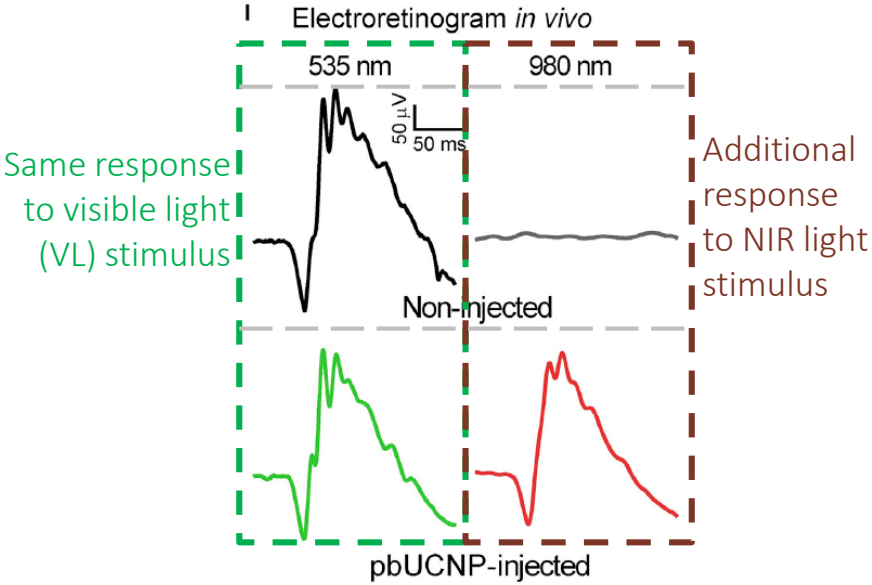
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Photoreceptor Activation**:

- Single rod pipette recordings on acutely dissected retinae
  - Amplitude and kinetics of photocurrents elicted by NIR vs VL were identical
  - No delay in response to NIR compared to VL
  - No alteration of light adaptation



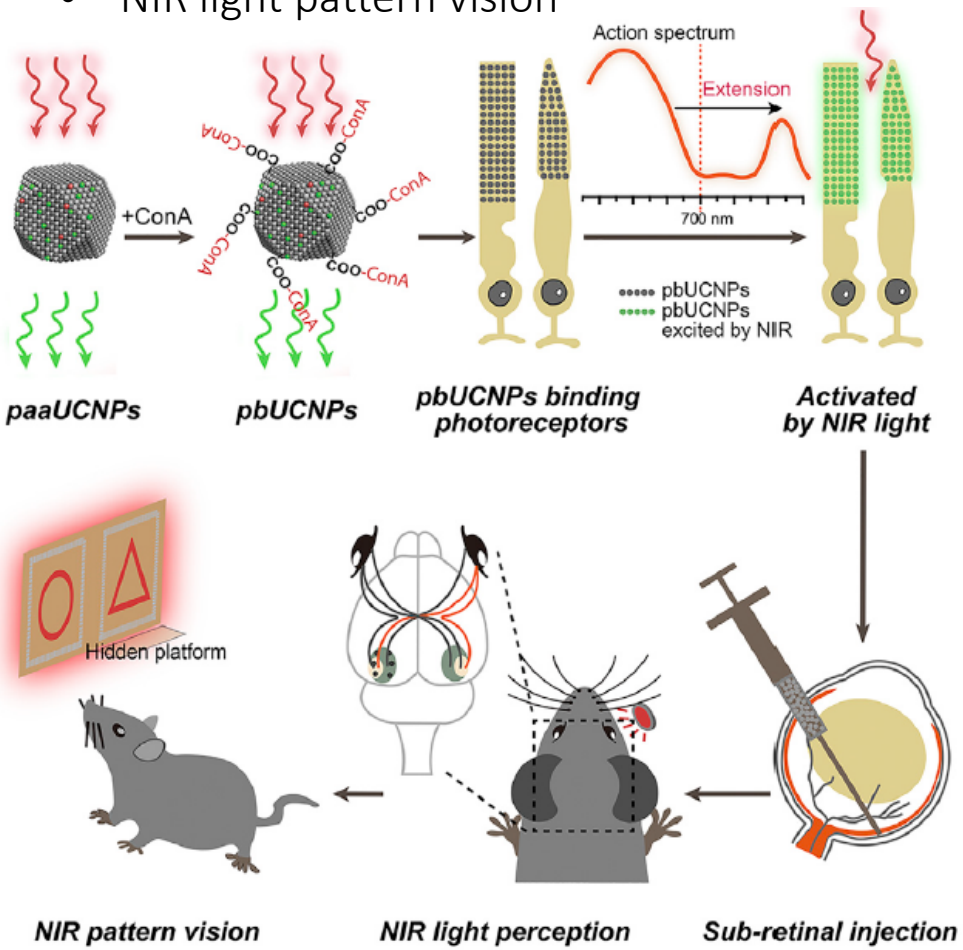
- Population response *in vivo* in ERG



photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Light Sensation** in the Mice:

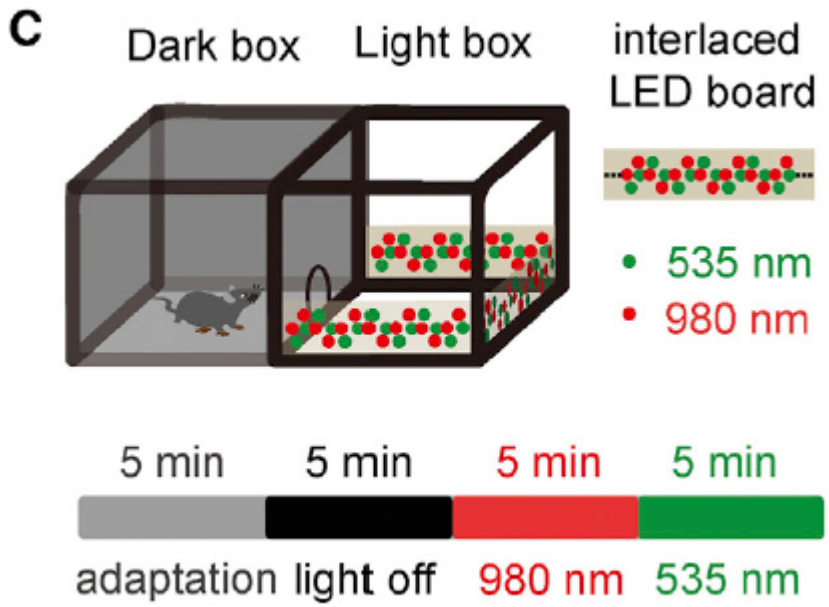
- Pupillary light reflexes upon NIR light stimulus → sub-conscious sensation
- Light-dark box experiments → conscious sensation
- Light-induced fear conditioning
- Recording visually evoked potentials (VEPs) in visual cortex
- NIR light pattern vision

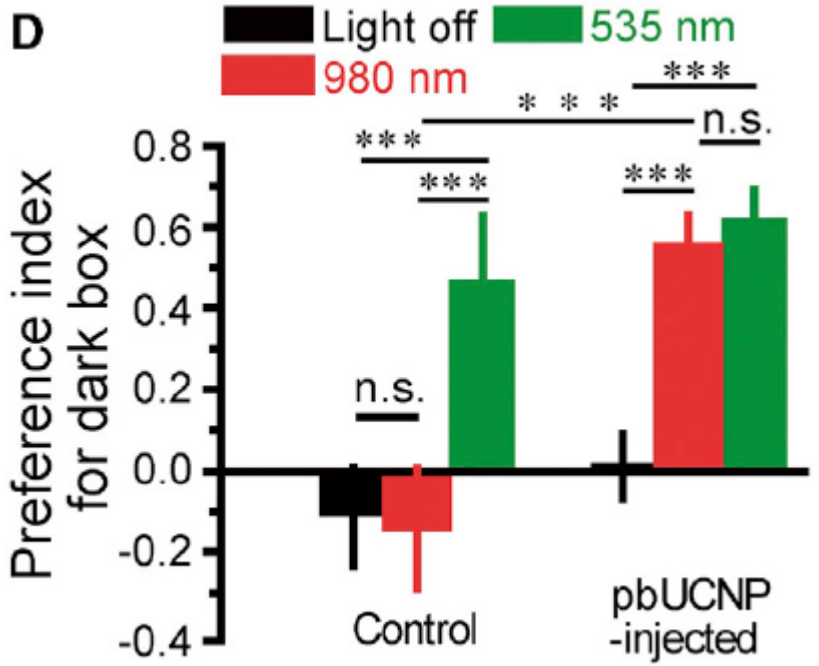


photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Light Sensation** in the Mice:

- Pupillary light reflexes upon NIR light stimulus → sub-conscious sensation
- **Light-dark box experiments** → conscious sensation
- Light-induced fear conditioning
- Recording visually evoked potentials (VEPs) in visual cortex
- NIR light pattern vision



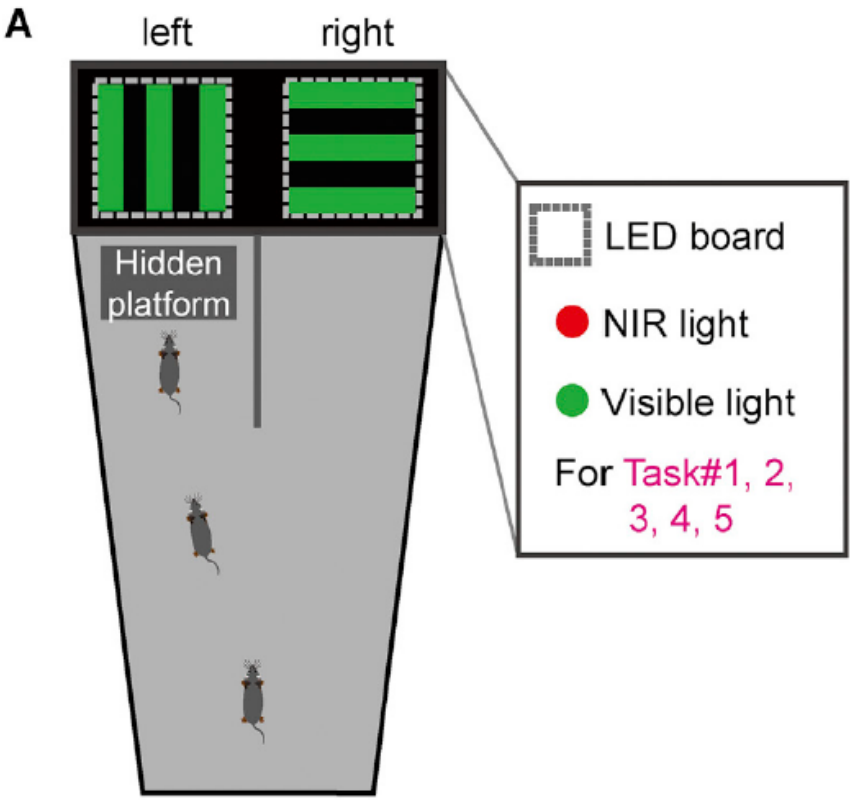


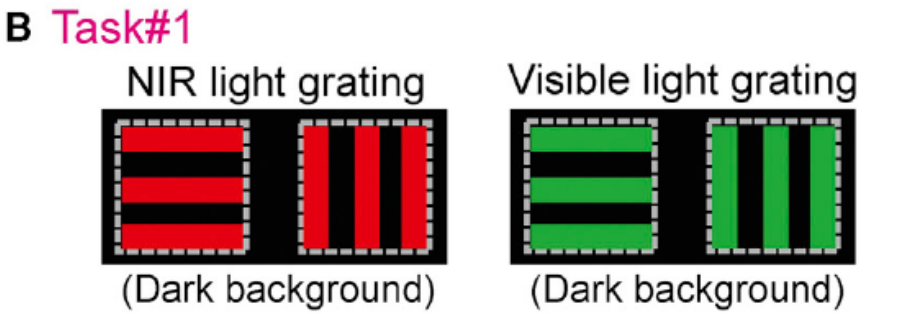
- All mice prefer dark box over VL illuminated box
- pbUCNP injected mice chose dark box over NIR illuminated box
- Control mice had no preference in dark vs NIR illumination

photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Light Sensation** in the Mice:

- Pupillary light reflexes upon NIR light stimulus → sub-conscious sensation
- Light-dark box experiments → conscious sensation
- Light-induced fear conditioning
- Recording visually evoked potentials (VEPs) in visual cortex
- **NIR light pattern vision**



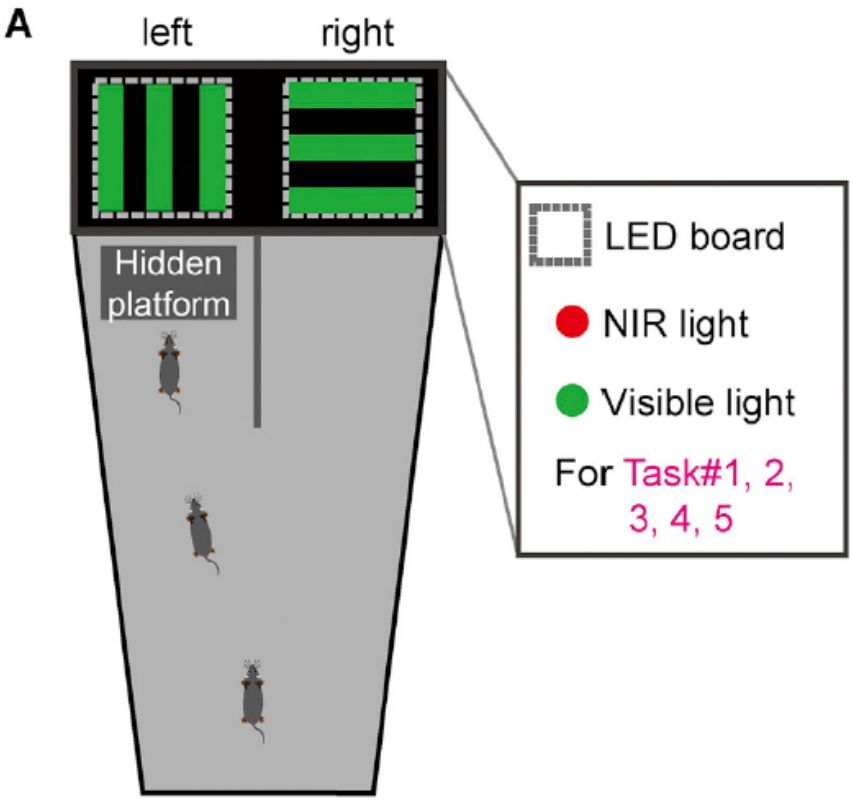


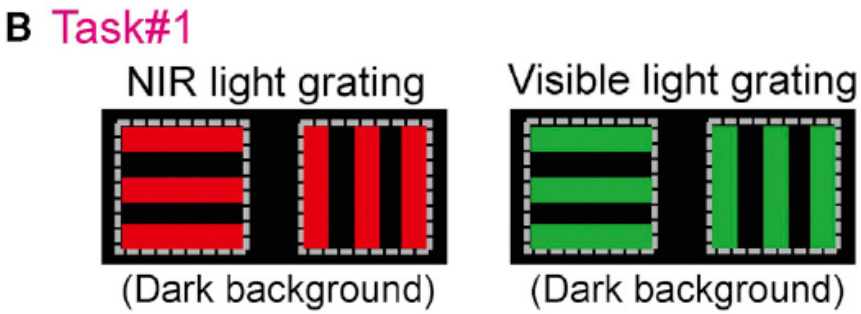
Water maze with platform associated with a light pattern

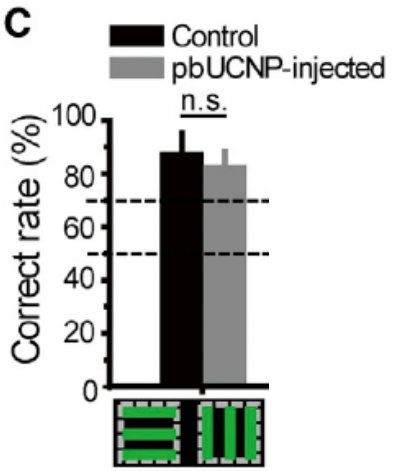
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Light Sensation** in the Mice:

- Pupillary light reflexes upon NIR light stimulus → sub-conscious sensation
- Light-dark box experiments → conscious sensation
- Light-induced fear conditioning
- Recording visually evoked potentials (VEPs) in visual cortex
- **NIR light pattern vision**







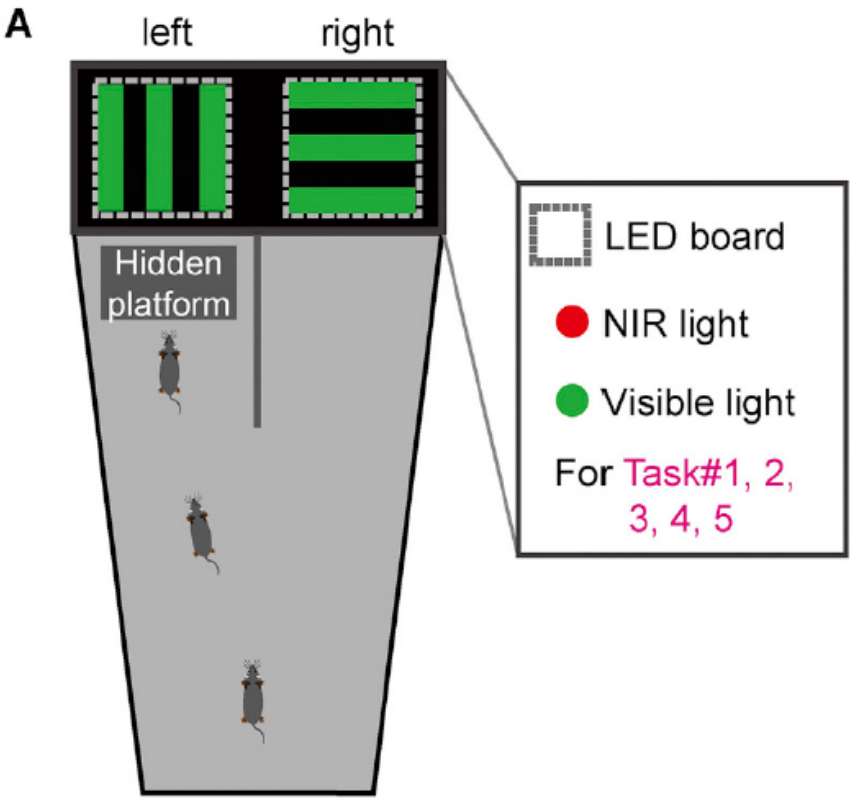
Water maze with platform associated with a light pattern

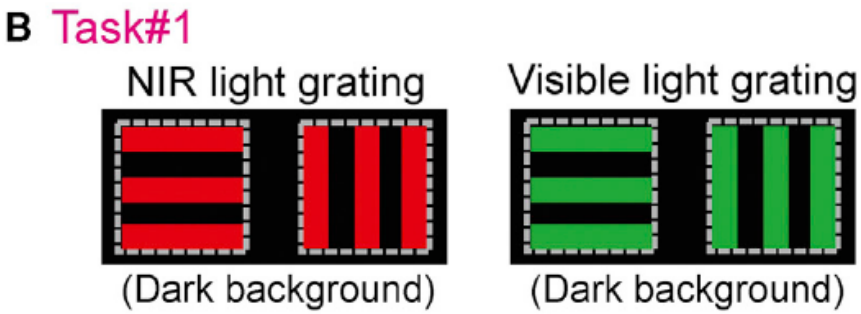
- All mice find VL grating platform

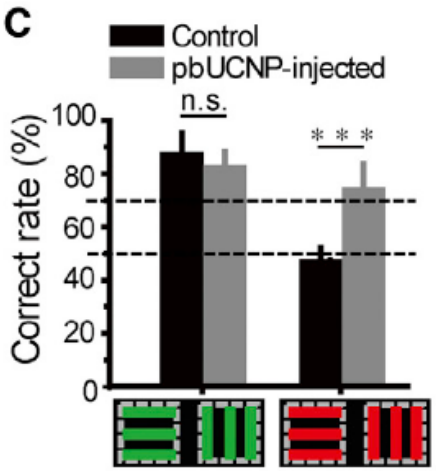
photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Assessment of **Light Sensation** in the Mice:

- Pupillary light reflexes upon NIR light stimulus → sub-conscious sensation
- Light-dark box experiments → conscious sensation
- Light-induced fear conditioning
- Recording visually evoked potentials (VEPs) in visual cortex
- **NIR light pattern vision**







Water maze with platform associated with a light pattern

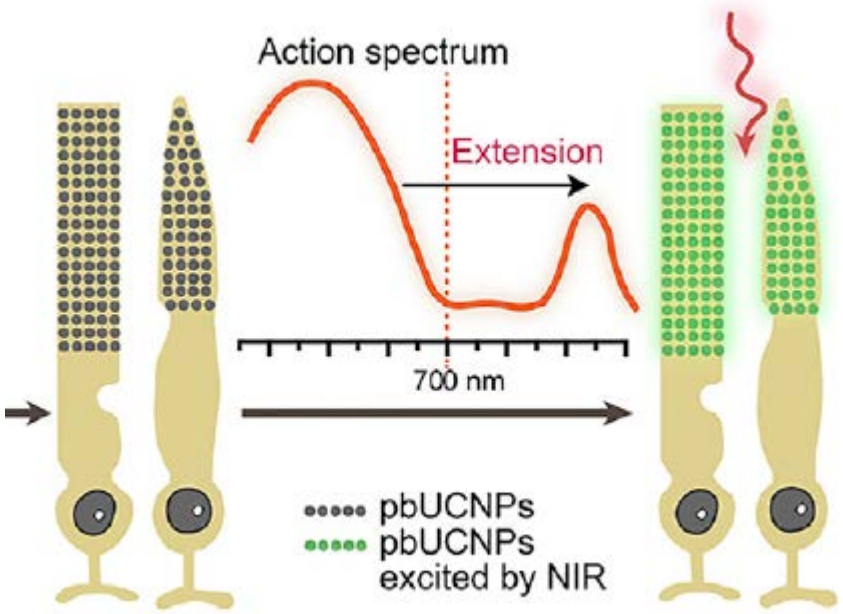
- All mice find VL grating platform
- pbUCNP injected mice find NIR grating platform
- Control mice chose NIR grating platforms randomly

photoreceptor-binding upconversion nanoparticles (pbUCNPs)

→ Successful extension of the visible light spectrum towards NIR WLs by using nanoantennae added to endogenous visual system

→ Both VL and NIR can be seen simultaneously

→ Applications in visual repair and enhancement

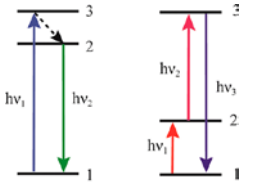


Photon upconversion (UC)

CHEMICAL REVIEWS
Review
pubs.acs.org/CR

Upconversion Luminescent Materials: Advances and Applications

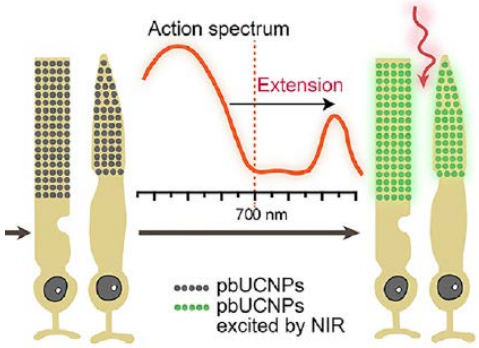
Jing Zhou,[†] Qian Liu,[†] Wei Feng, Yun Sun, and Fuyou Li*



Article
Cell

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

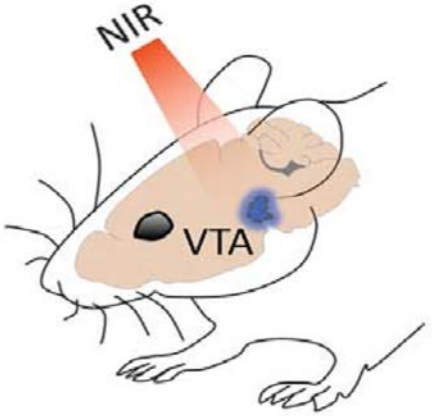
Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]



NEUROSCIENCE

Near-infrared deep brain stimulation via upconversion nanoparticle-mediated optogenetics

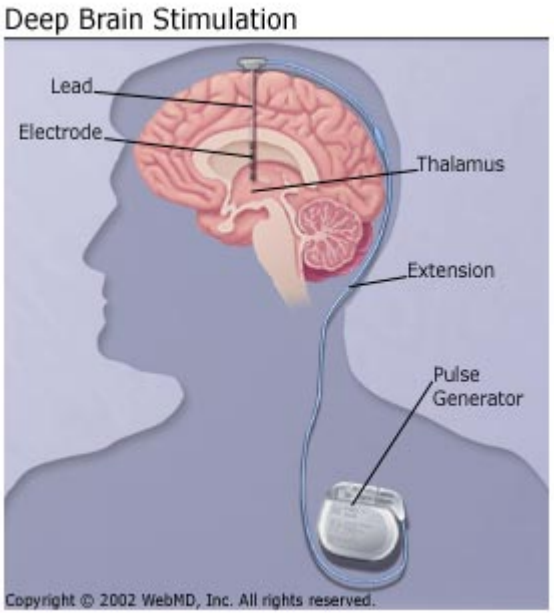
Shuo Chen,[1*] Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9*] Thomas J. McHugh[1,10*]



NEUROSCIENCE

Near-infrared deep brain stimulation via upconversion nanoparticle–mediated optogenetics

Shuo Chen,[1]* Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9]* Thomas J. McHugh[1,10]*



https://www.webmd.com/parkinsons-disease/guide/dbs-parkinsons

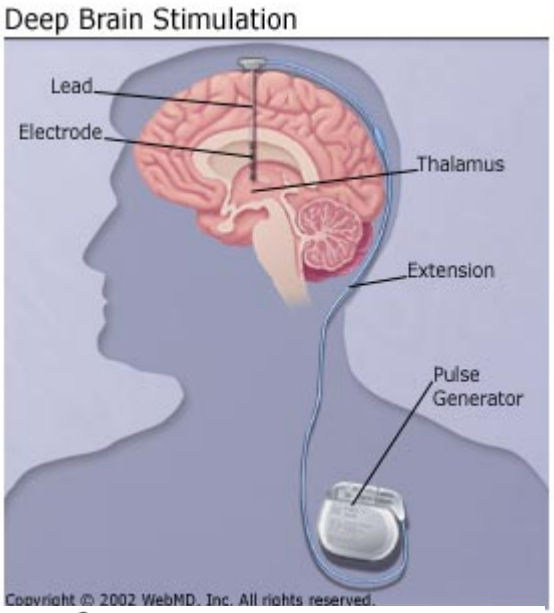
Deep brain stimulation

- Promising therapeutic options (e.g. Parkinson's)
- Permanently implanted electrodes
- Non-specific activation of neurons

NEUROSCIENCE

Near-infrared deep brain stimulation via upconversion nanoparticle–mediated optogenetics

Shuo Chen,[1]* Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9]* Thomas J. McHugh[1,10]*



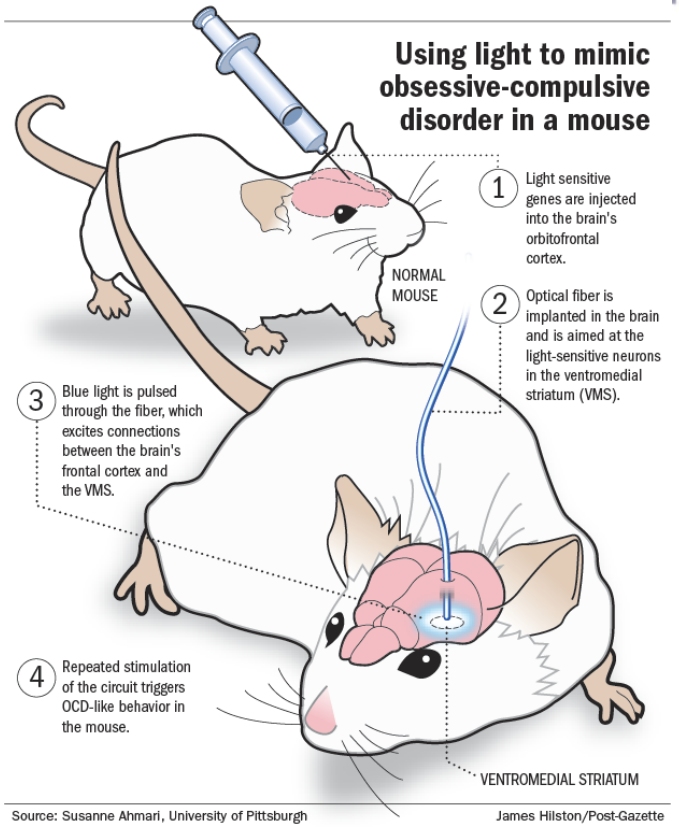
https://www.webmd.com/parkinsons-disease/guide/dbs-parkinsons

Deep brain stimulation

- Promising therapeutic options (e.g. Parkinson's)
- Permanently implanted electrodes
- Non-specific activation of neurons

Optogenetics

- Cell-specific expression of light activated channels
- Invasive optical fibres (light scattering and absorption)

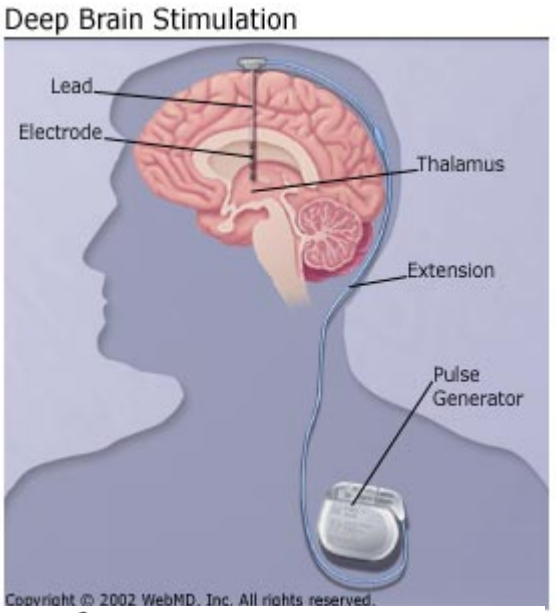


https://www.post-gazette.com/news/health/2015/02/01/Pittsburgh-researchers-use-light-on-animal-brains-to-study-mental-disorders/stories/201502010006

NEUROSCIENCE

Near-infrared deep brain stimulation via upconversion nanoparticle–mediated optogenetics

Shuo Chen,[1]* Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9]* Thomas J. McHugh[1,10]*



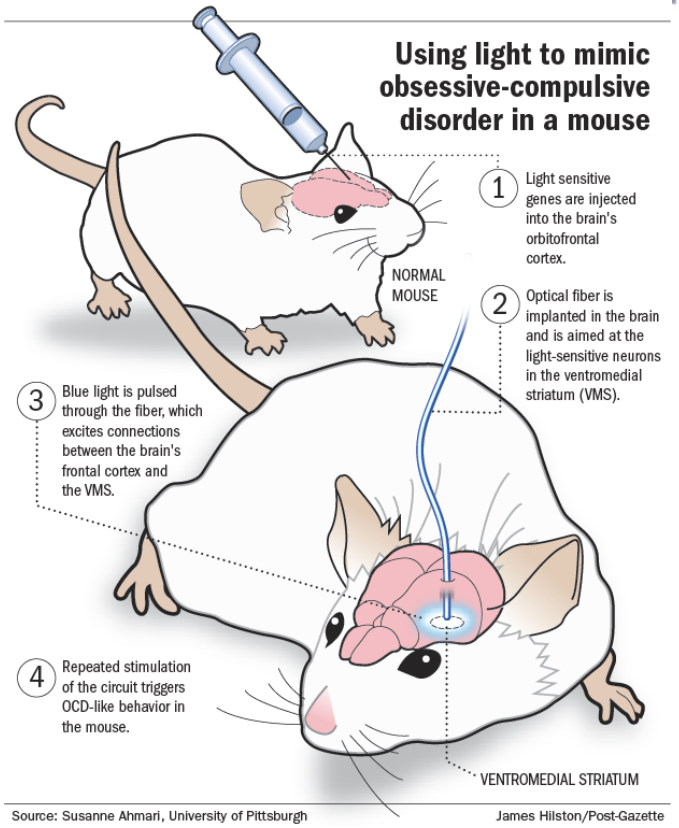
https://www.webmd.com/parkinsons-disease/guide/dbs-parkinsons

Deep brain stimulation

- Promising therapeutic options (e.g. Parkinson's)
- Permanently implanted electrodes
- Non-specific activation of neurons

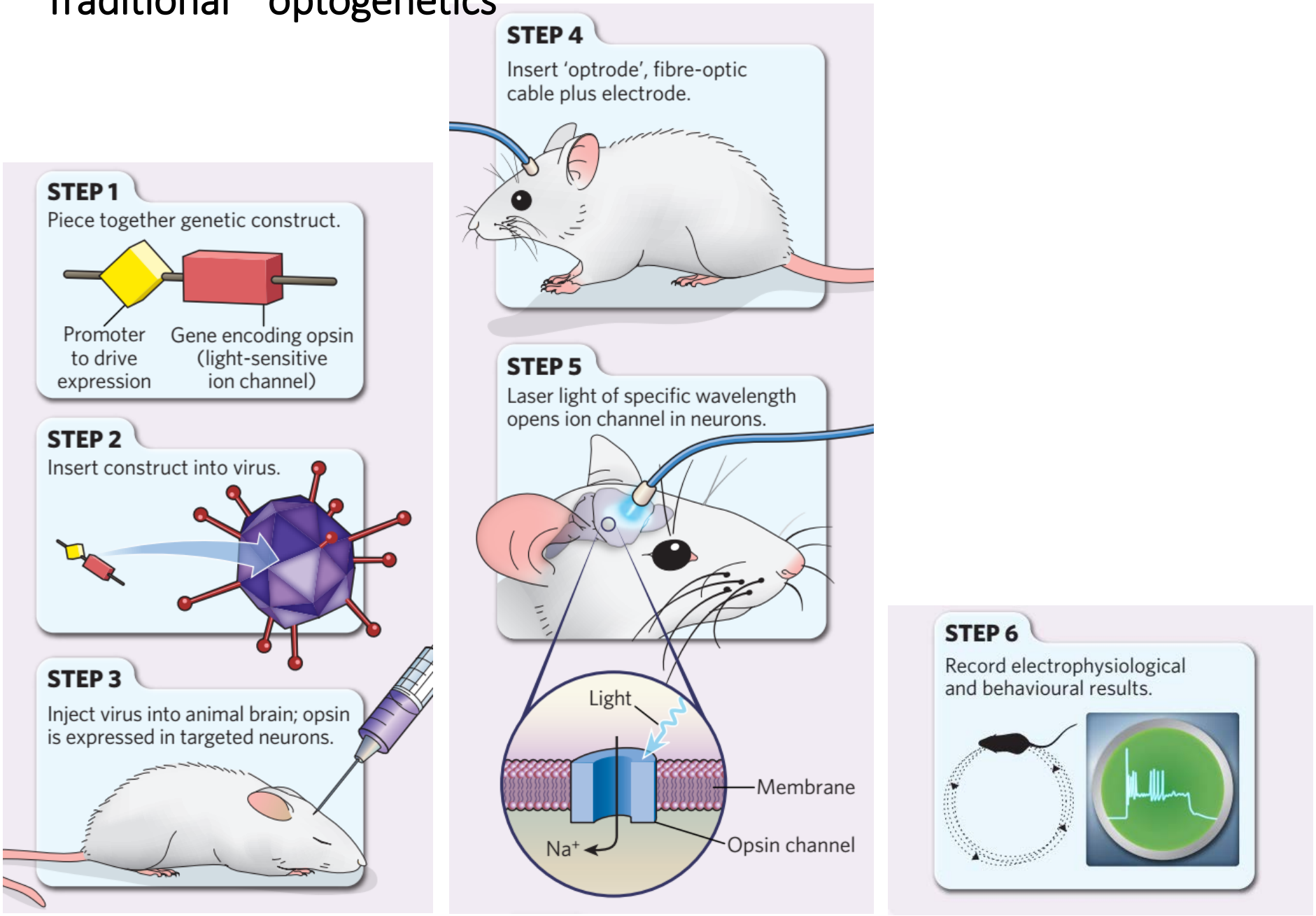
Optogenetics

- Cell-specific expression of light activated channels
- Invasive optical fibres (light scattering and absorption)
- Maximum penetration depth is possible with NIR light
  But low energy cannot activate channels
- Two-photon optogenetics only in shallow brain areas (scattering)



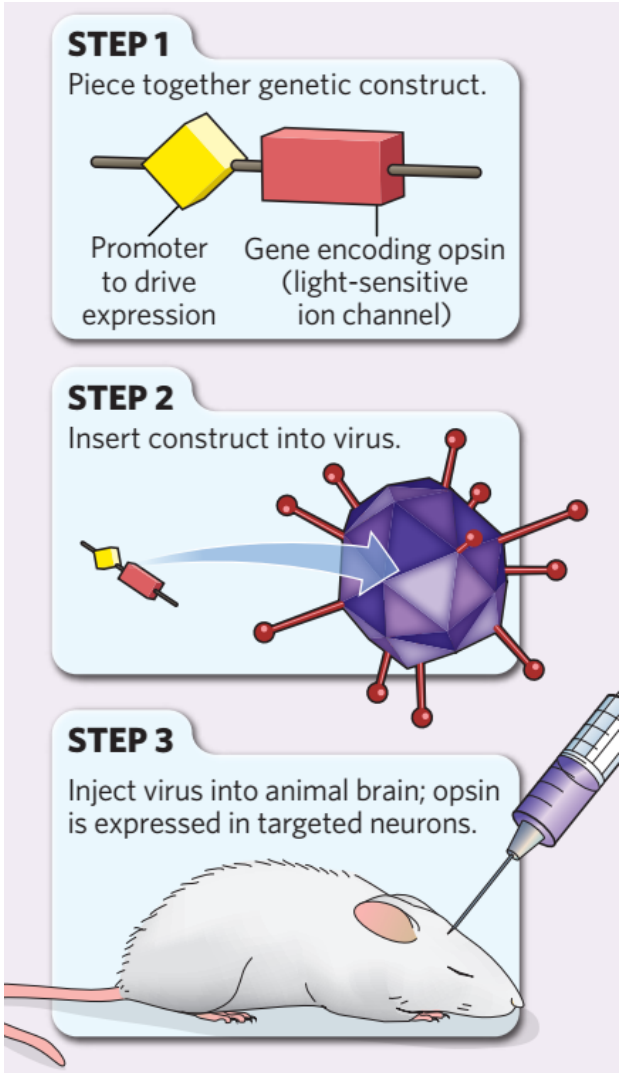
https://www.post-gazette.com/news/health/2015/02/01/Pittsburgh-researchers-use-light-on-animal-brains-to-study-mental-disorders/stories/201502010006

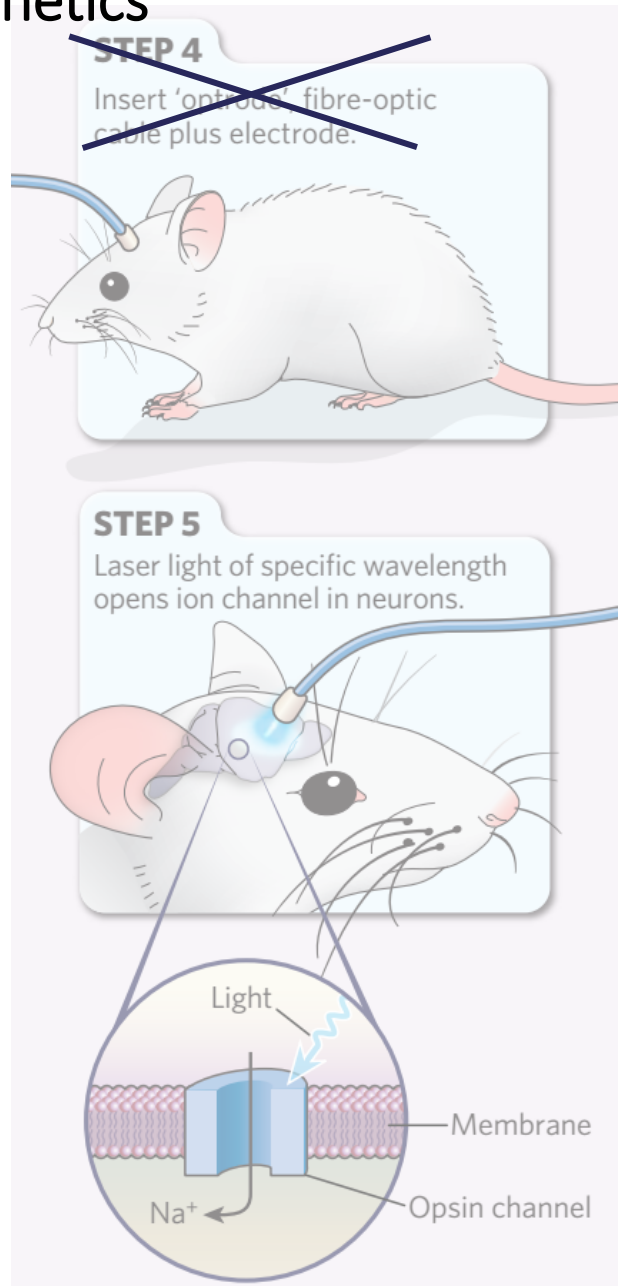
“Traditional” optogenetics

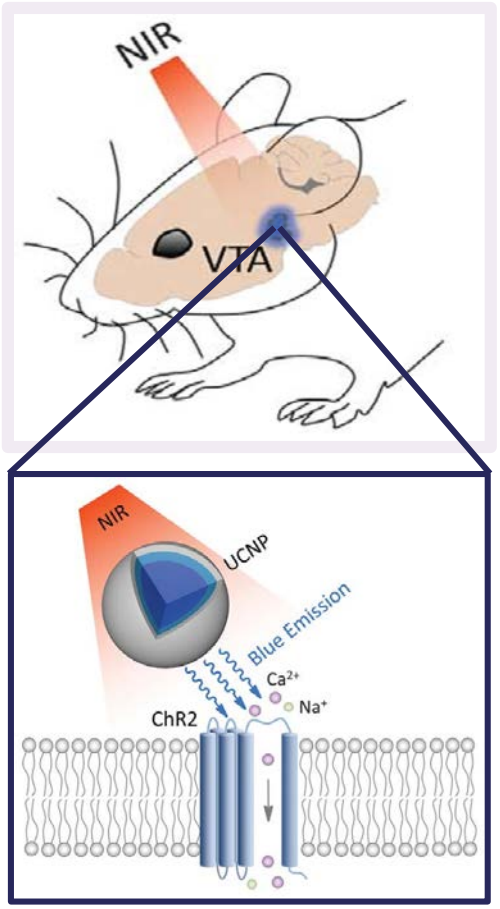


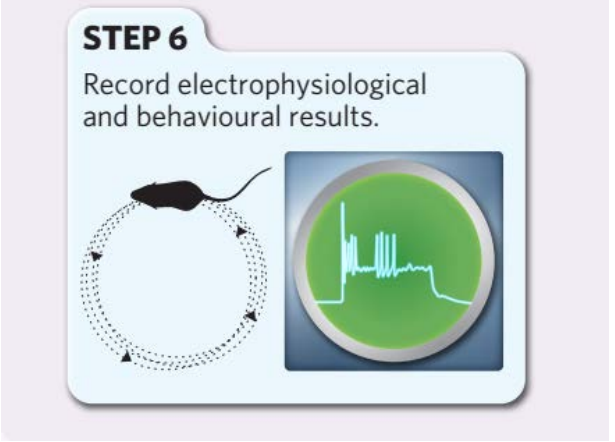
L. Buchen (2010), Nature, doi:10.1038/465026a

UCNP-mediated optogenetics



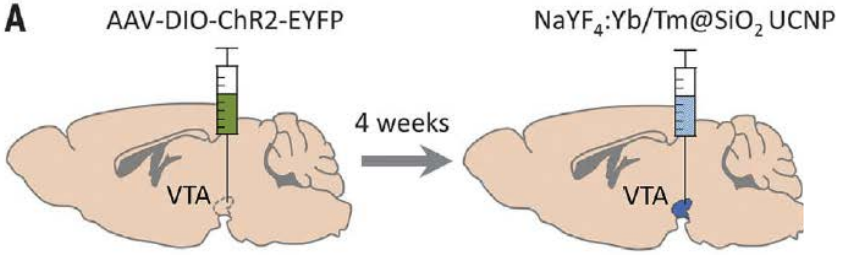






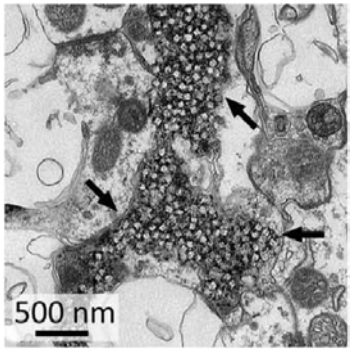
L. Buchen (2010), Nature, doi:10.1038/465026a

UCNP-mediated optogenetics

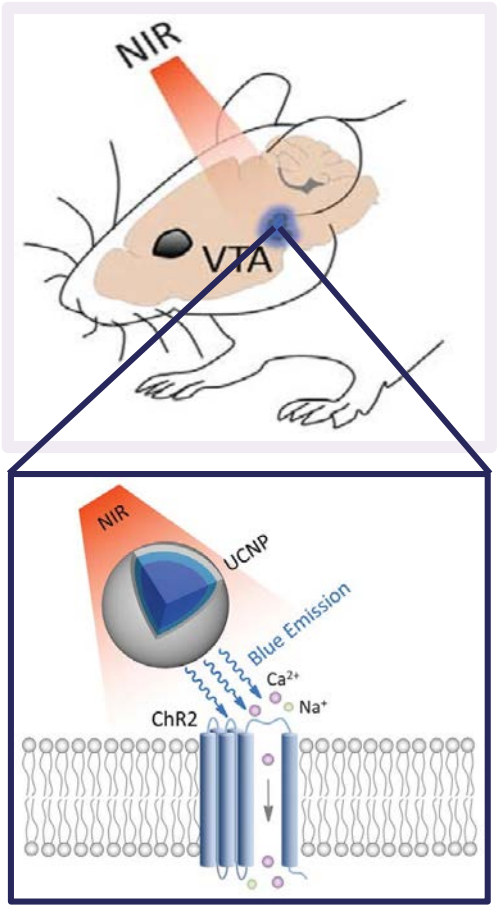


Injection of Virus carrying Light-sensitive channel

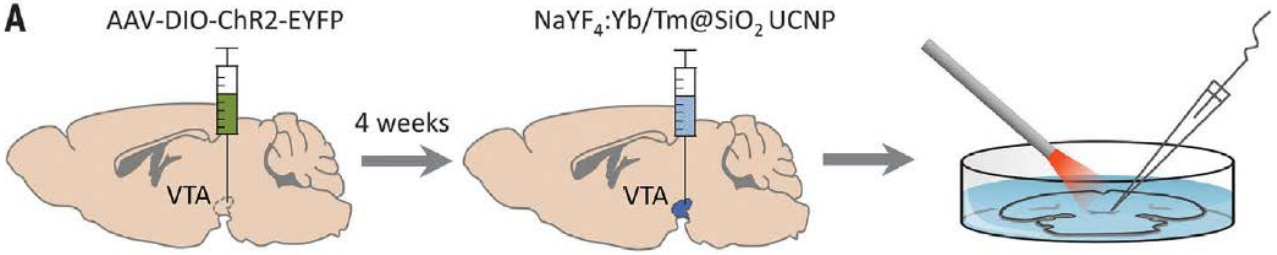
Injection of UCNPs



Extracellular localization of injected UCNPs



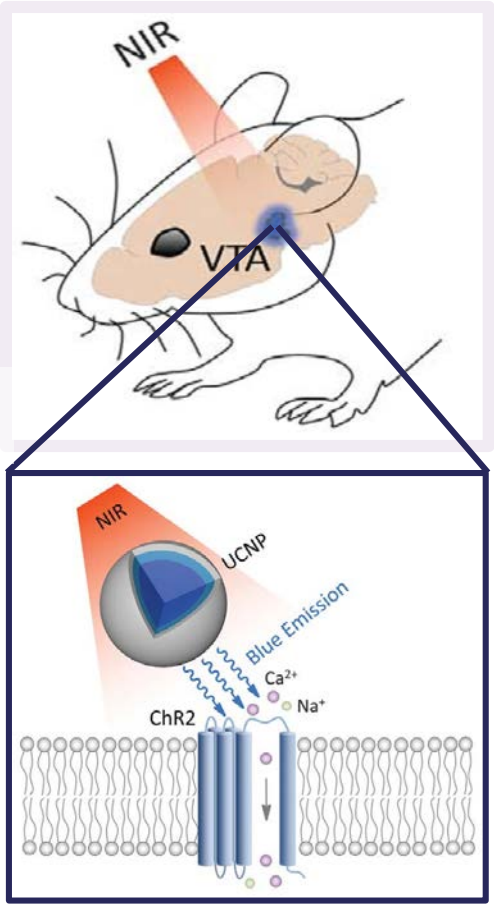
UCNP-mediated optogenetics

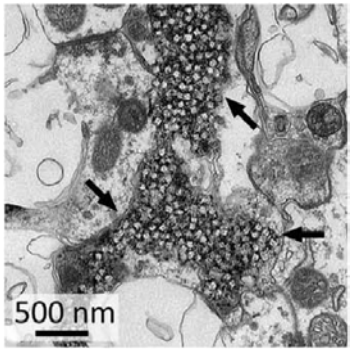


Injection of Virus carrying Light-sensitive channel

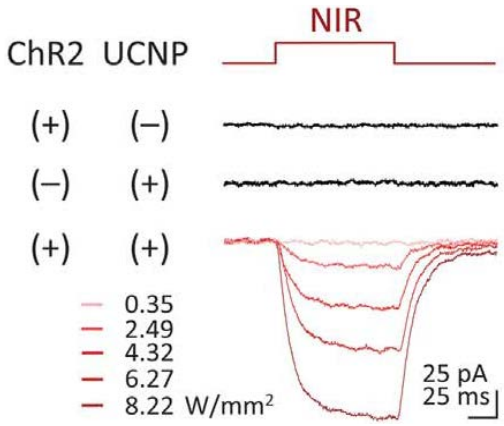
Injection of UCNPs

Whole cell recording in acute slice



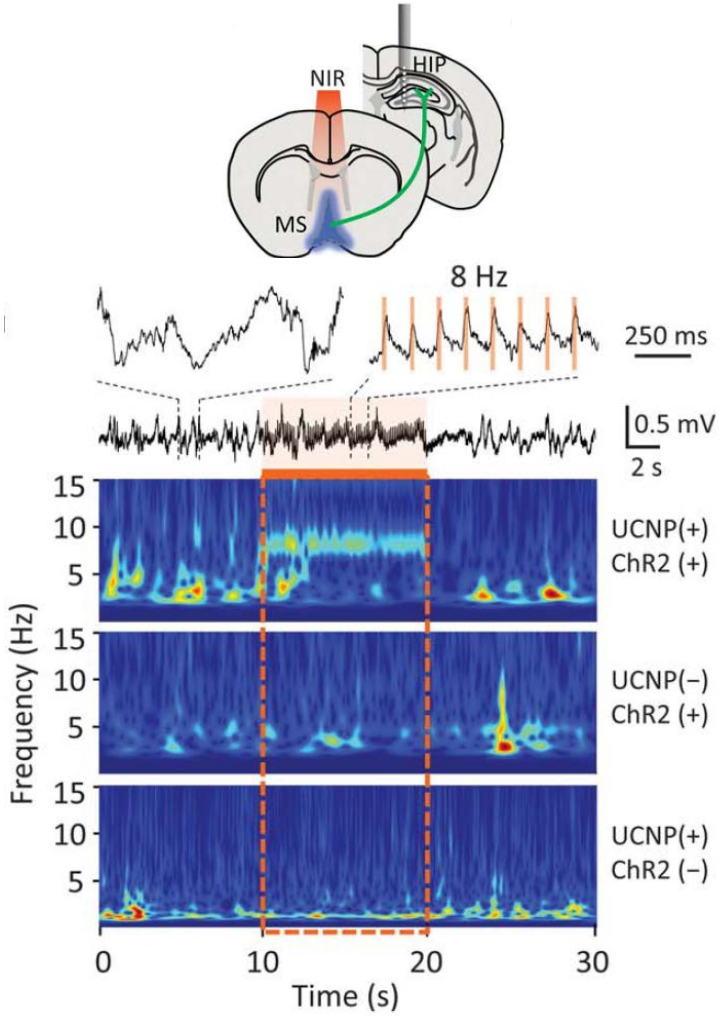


Extracellular localization of injected UCNPs

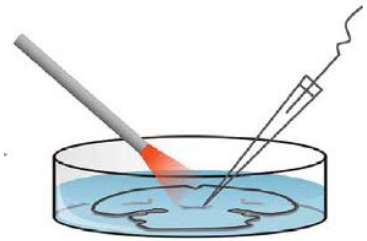


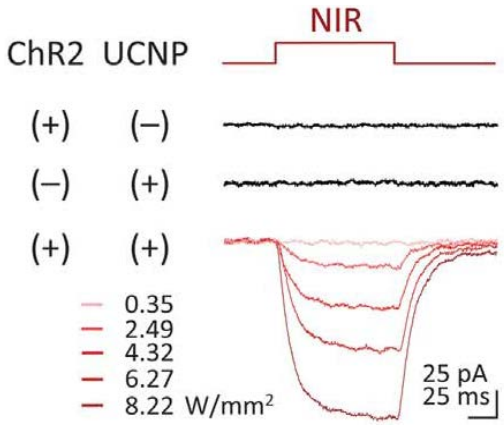
→ NIR evokes current in cells expressing both ChR2 and UCNP in laser intensity dependent manner

UCNP-mediated optogenetics

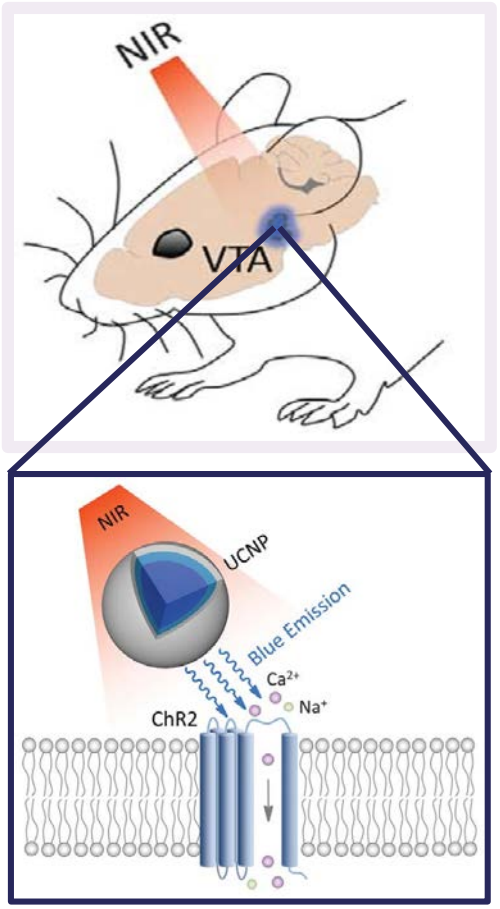


In vivo recordings of hippocampal local field potential (LFP)
→ Pulsed NIR stimulation entrained the hippocampal theta oscillation in a frequency-dependent manner

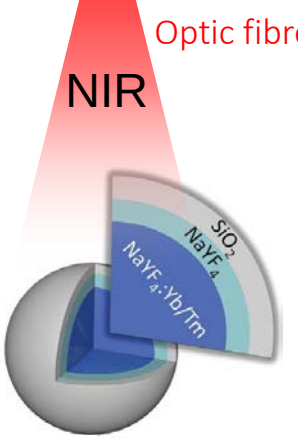


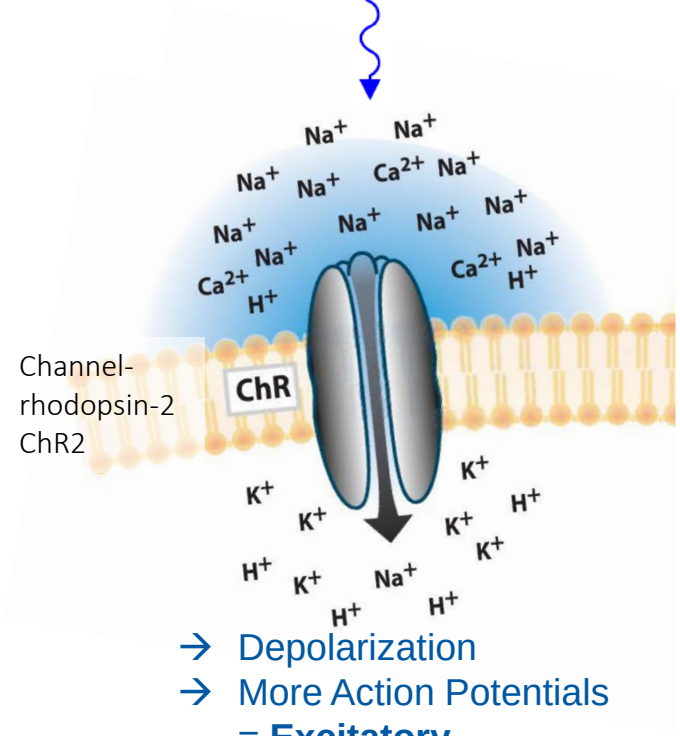


Whole cell recording in acute slice
→ NIR evokes current in cells expressing both ChR2 and UCNP in laser intensity dependent manner



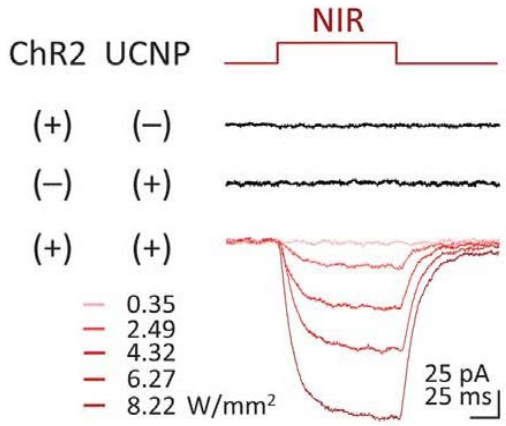
Optic fibre 2 mm above skull

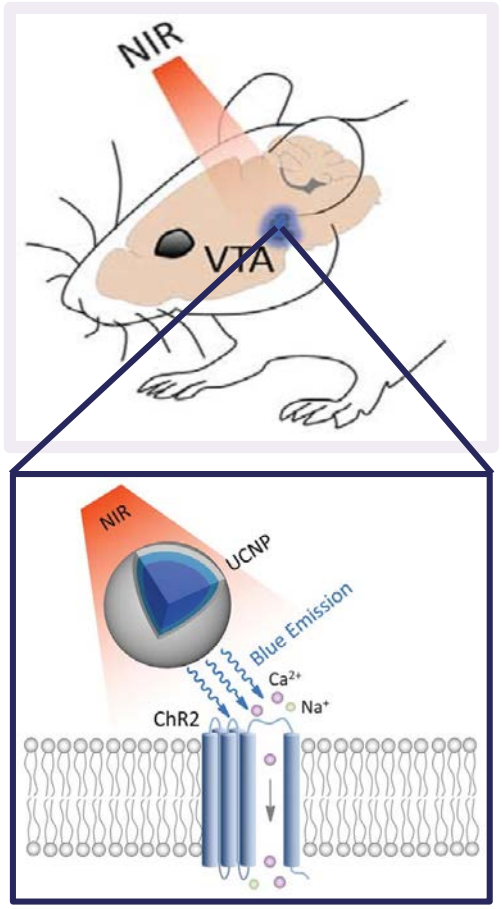




Channel-rhodopsin-2
ChR2

→ Depolarization
→ More Action Potentials
= **Excitatory**



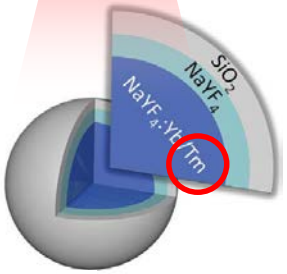


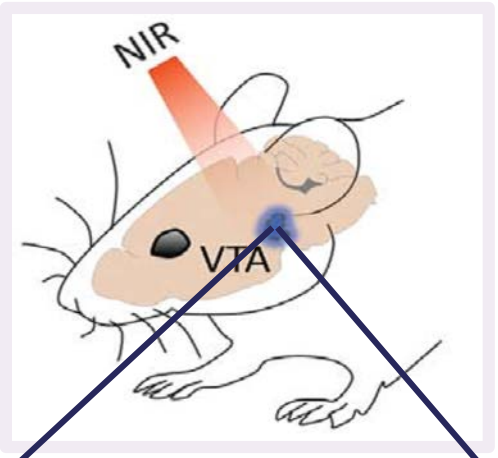
Modified from: Yizhar (2011), Neuron, https://doi.org/10.1016/j.neuron.2011.06.004

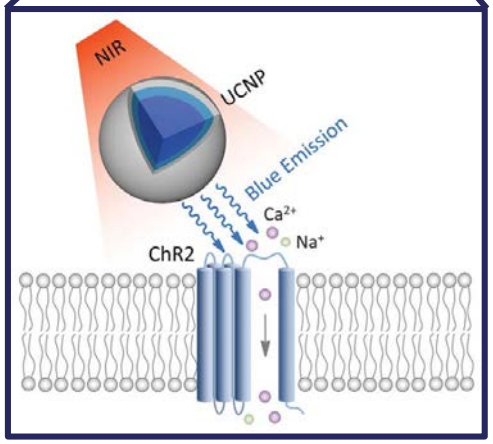
Optic fibre 2 mm above skull

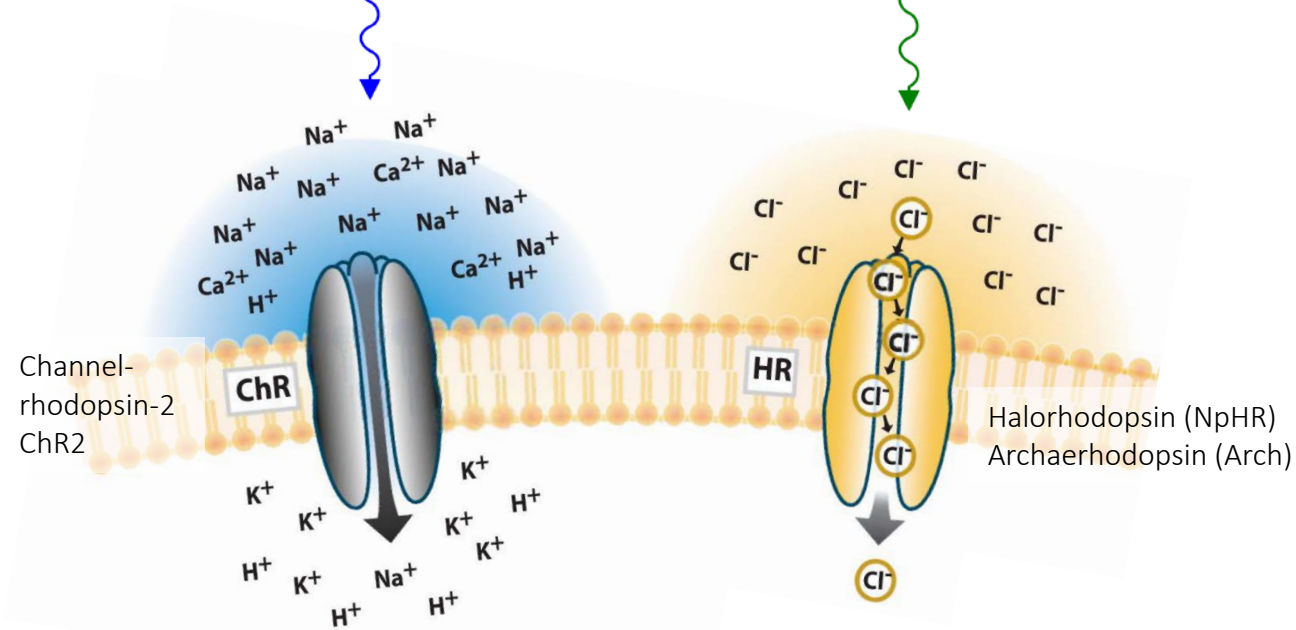
NIR

NIR









Channel-rhodopsin-2 ChR2

Halorhodopsin (NpHR)
Archaerhodopsin (Arch)

→ Depolarization
→ More Action Potentials
= **Excitatory**

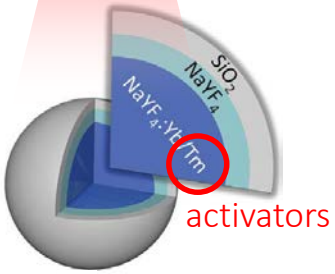
→ Hyperpolarization
→ Less Action Potentials
= **Inhibition**

Modified from: Yizhar (2011), Neuron, https://doi.org/10.1016/j.neuron.2011.06.004

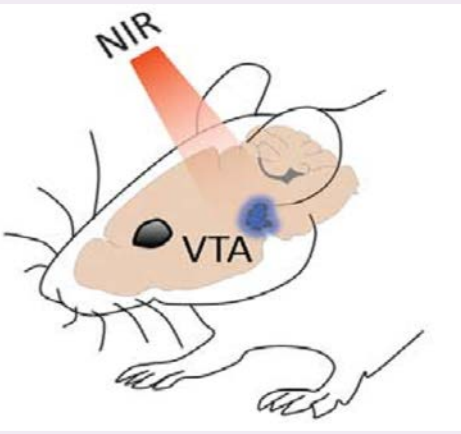
Optic fibre 2 mm above skull

NIR

NIR



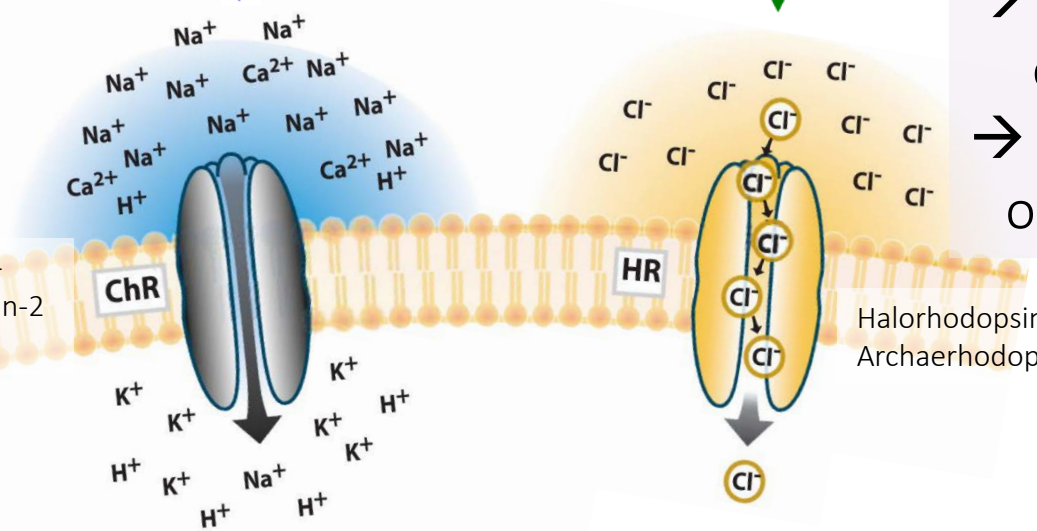
activators



Incorporation of another element into the UCNP **shifts emission WL**

→ Specific activation of one type of channel

→ Specific **activation or inhibition** of specific neuron



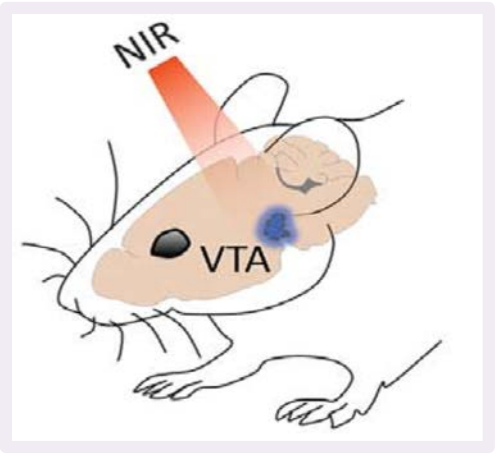
Channel-rhodopsin-2 ChR2

Halorhodopsin (NpHR)
Archaerhodopsin (Arch)

→ Depolarization
→ More Action Potentials
= **Excitatory**

→ Hyperpolarization
→ Less Action Potentials
= **Inhibition**

Modified from: Yizhar (2011), Neuron, https://doi.org/10.1016/j.neuron.2011.06.004

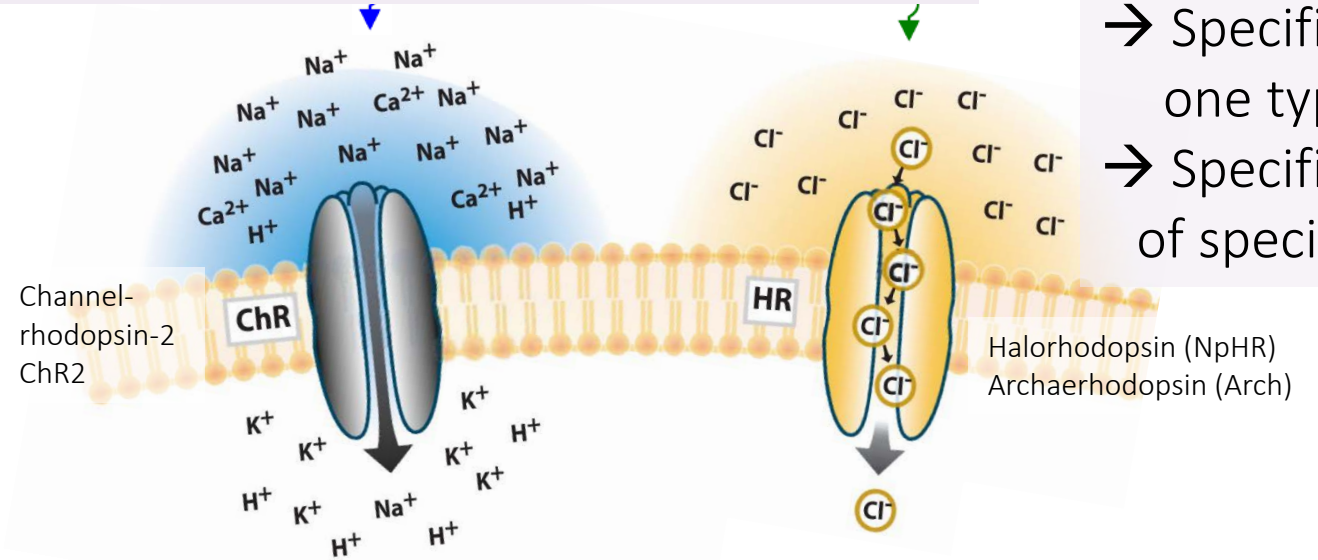


Biocompatibility further optimized by Silica Coating (NaYF4:Yb/Tm@SiO2)

Incorporation of another element into the UCNP **shifts emission WL**

→ Specific activation of one type of channel

→ Specific **activation or inhibition** of specific neuron



Channel-rhodopsin-2 ChR2

Halorhodopsin (NpHR)
Archaerhodopsin (Arch)

→ Depolarization
→ More Action Potentials
= **Excitatory**

→ Hyperpolarization
→ Less Action Potentials
= **Inhibition**

Modified from: Yizhar (2011), Neuron, https://doi.org/10.1016/j.neuron.2011.06.004

In vivo alteration of behaviour using UCNP-mediated optogenetics

LETTER

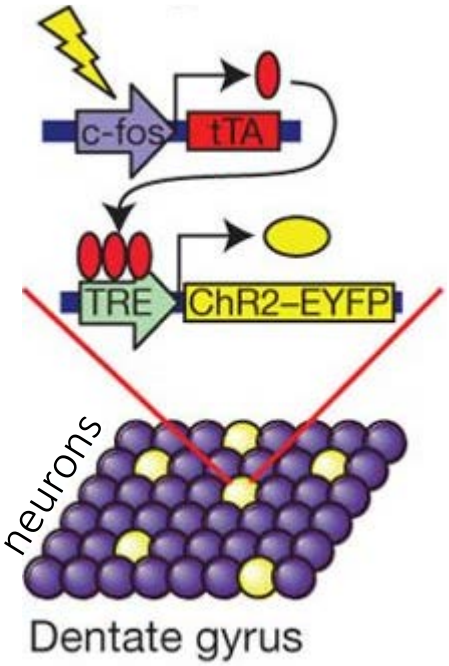
doi:10.1038/nature11028

Optogenetic stimulation of a hippocampal engram activates fear memory recall

Xu Liu[1]*, Steve Ramirez[1]*, Petti T. Pang[1], Corey B. Puryear[1], Arvind Govindarajan[1], Karl Deisseroth[2] & Susumu Tonegawa[1]

- Memory (engram) = encoded by a sparse population of neurons
- Neurons can be tagged during learning
- Activation of those neurons → respective behavioural output
  E.g. freezing in fear conditioning
- Here: optogenetic reactivation of hippocampal neurons activated during fear conditioning induces freezing behaviour

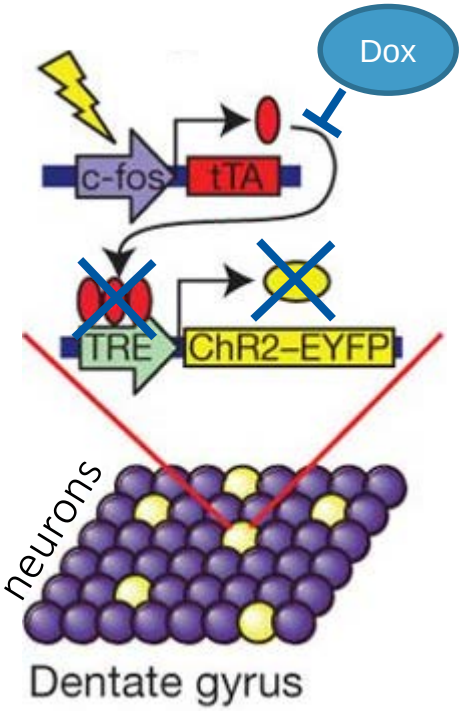
In vivo alteration of behaviour using UCNP-mediated optogenetics



- C-fos is expressed upon neuronal activity
- Mice carry tetracycline transcriptional activator (tTA) under c-fos promotor
- tTA binds tetracycline-responsive element (TRE) site, triggering expression of Channelrhodopsin (ChR2, tagged with EYFP)

Xu Liu (2012) Nature Letter, doi:10.1038/nature11028

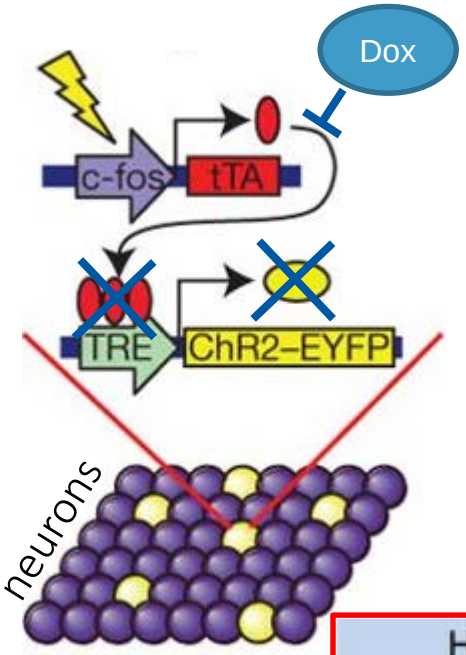
In vivo alteration of behaviour using UCNP-mediated optogenetics



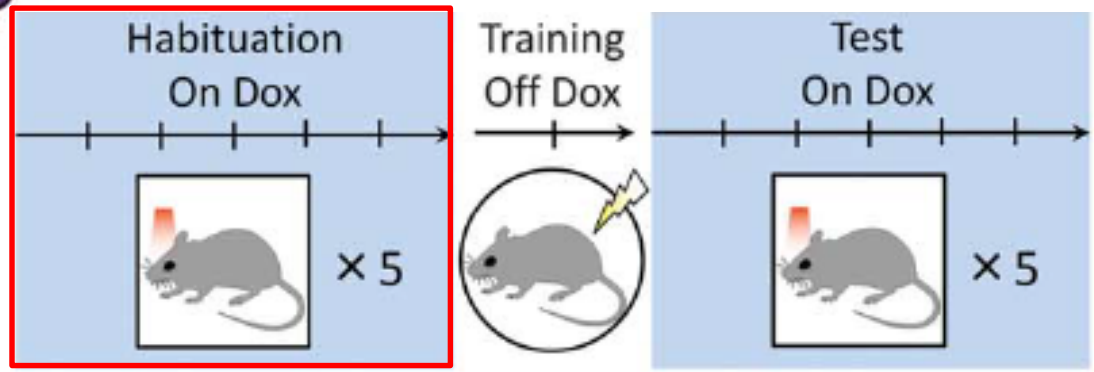
- C-fos is expressed upon neuronal activity
- Mice carry tetracycline transcriptional activator (tTA) under c-fos promotor
- tTA binds tetracycline-responsive element (TRE) site, triggering expression of Channelrhodopsin (ChR2, tagged with EYFP)
- Tetracycline Off System: +Doxicycline = no ChR expression

Xu Liu (2012) Nature Letter, doi:10.1038/nature11028

In vivo alteration of behaviour using UCNP-mediated optogenetics



- C-fos is expressed upon neuronal activity
- Mice carry tetracycline transcriptional activator (tTA) under c-fos promotor
- tTA binds tetracycline-responsive element (TRE) site, triggering expression of Channelrhodopsin (ChR2, tagged with EYFP)
- Tetracycline Off System: +Doxicycline = no ChR expression

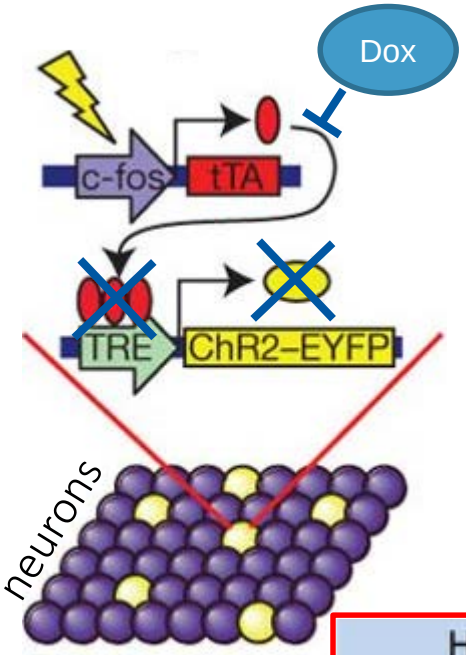


- No ChR-expression (+Dox)
- UCNP have been injected (but no effect, as no channel)

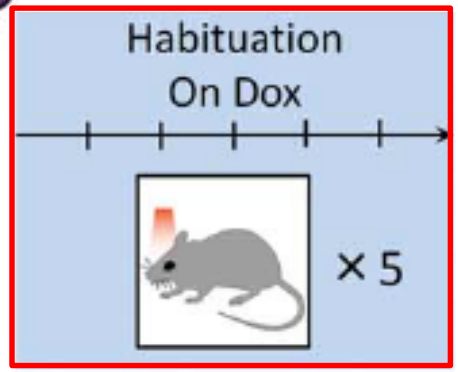
- Environment A: freezing reaction upon NIR illumination is tested

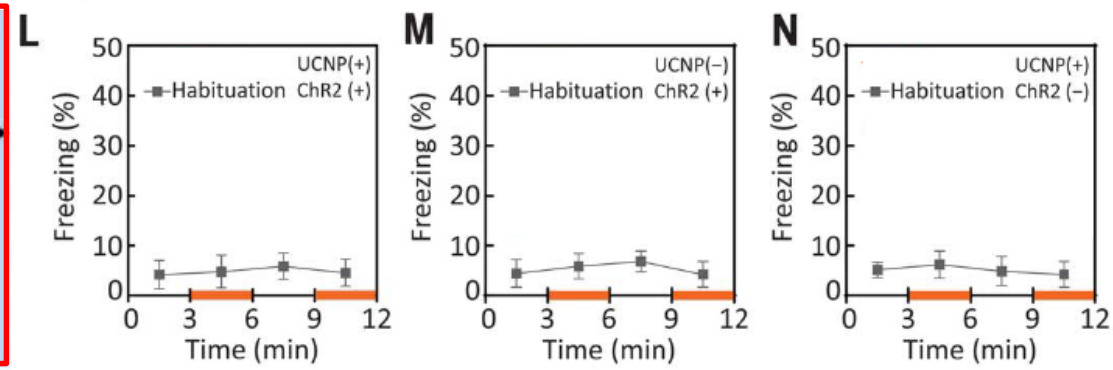
Xu Liu (2012) Nature Letter, doi:10.1038/nature11028

In vivo alteration of behaviour using UCNP-mediated optogenetics



- C-fos is expressed upon neuronal activity
- Mice carry tetracycline transcriptional activator (tTA) under c-fos promotor
- tTA binds tetracycline-responsive element (TRE) site, triggering expression of Channelrhodopsin (ChR2, tagged with EYFP)
- Tetracycline Off System: +Doxicycline = no ChR expression



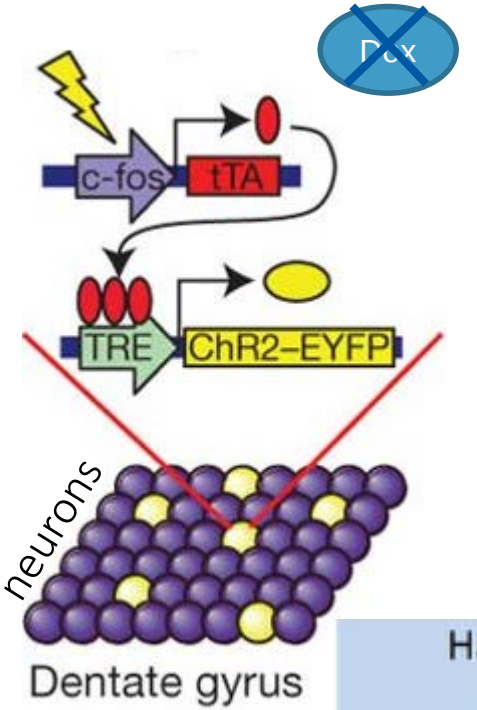


- No ChR-expression (+Dox)
- UCNP have been injected (but no effect, as no channel)

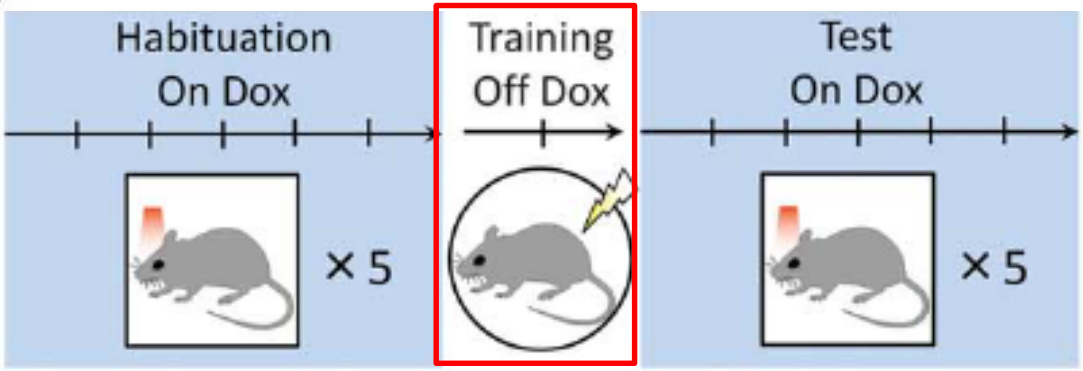
- Environment A: freezing reaction upon NIR illumination is tested

Xu Liu (2012) Nature Letter, doi:10.1038/nature11028

In vivo alteration of behaviour using UCNP-mediated optogenetics



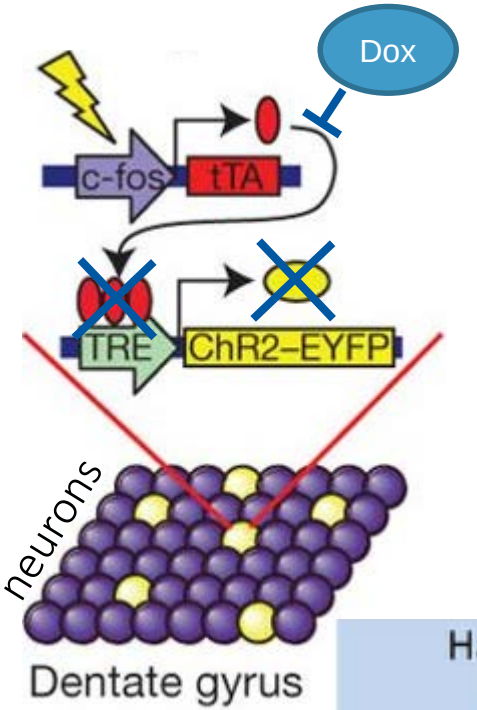
- C-fos is expressed upon neuronal activity
- Mice carry tetracycline transcriptional activator (tTA) under c-fos promotor
- tTA binds tetracycline-responsive element (TRE) site, triggering expression of Channelrhodopsin (ChR2, tagged with EYFP)
- Tetracycline Off System: +Doxicycline = no ChR expression



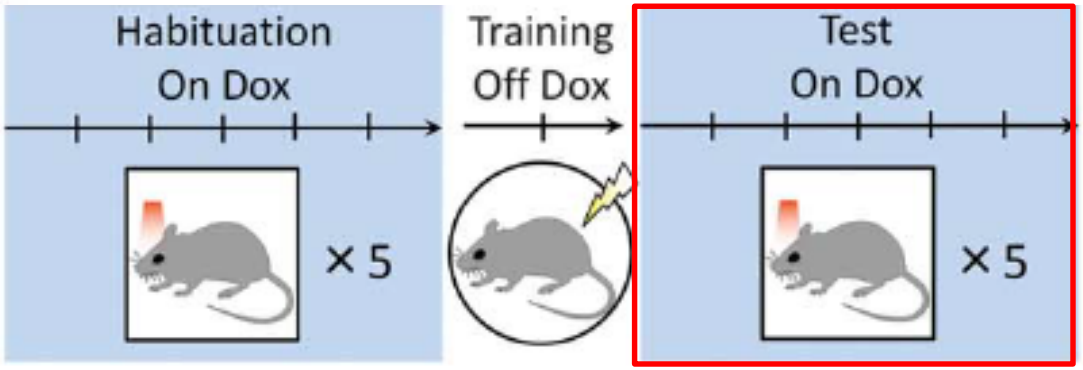
- Training in environment B: fear conditioning using electric shocks
- ChR-expression in the active neurons (-Dox)
- UCNP have been injected before (but no effect, as no NIR illumination)

Xu Liu (2012) Nature Letter, doi:10.1038/nature11028

In vivo alteration of behaviour using UCNP-mediated optogenetics



- C-fos is expressed upon neuronal activity
- Mice carry tetracycline transcriptional activator (tTA) under c-fos promotor
- tTA binds tetracycline-responsive element (TRE) site, triggering expression of Channelrhodopsin (ChR2, tagged with EYFP)
- Tetracycline Off System: +Doxicycline = no ChR expression

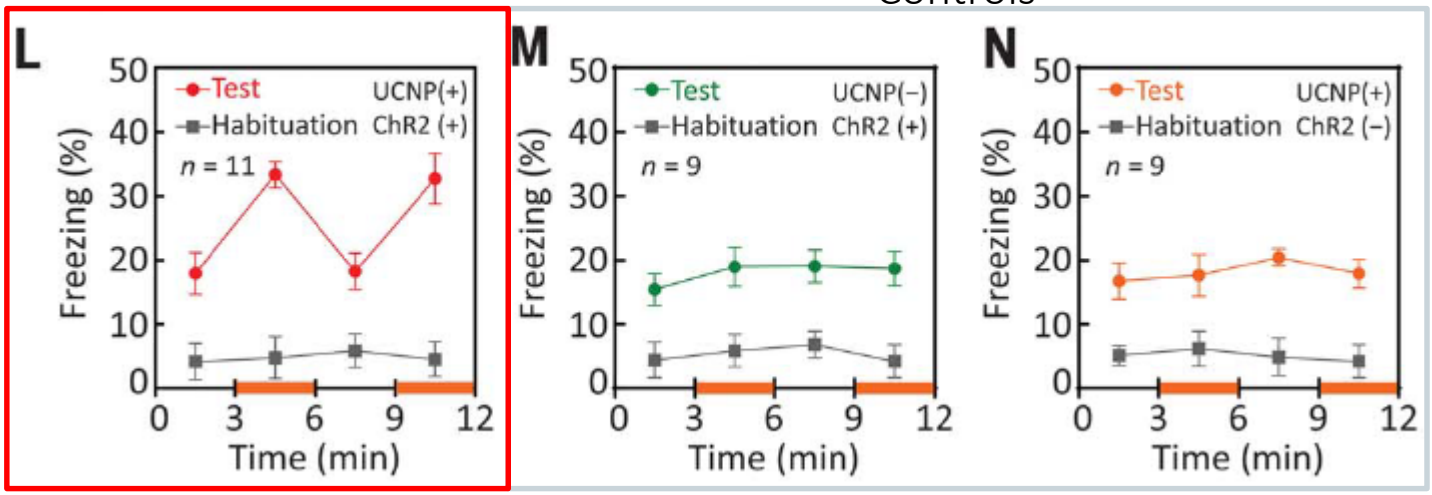


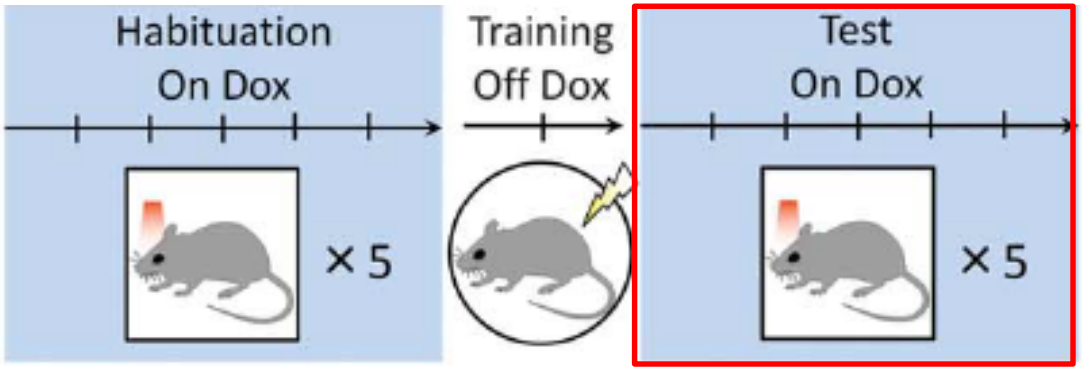
- No new ChR-expression (+Dox) → only the cells that have been active during fear conditioning, are equipped with channels
- UCNP have been injected before → freezing reaction upon NIR illumination is tested
- Environment A: is not associated with fear

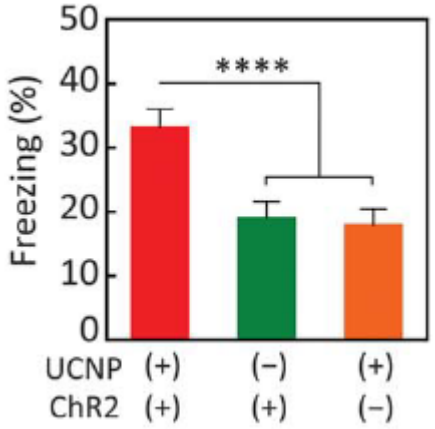
Xu Liu (2012) Nature Letter, doi:10.1038/nature11028

In vivo alteration of behaviour using UCNP-mediated optogenetics

Controls







- No new ChR-expression (+Dox) → only the cells that have been active during fear conditioning, are equipped with channels
- UCNP have been injected before → **freezing reaction upon NIR illumination is elevated**
- Environment A: is not associated with fear

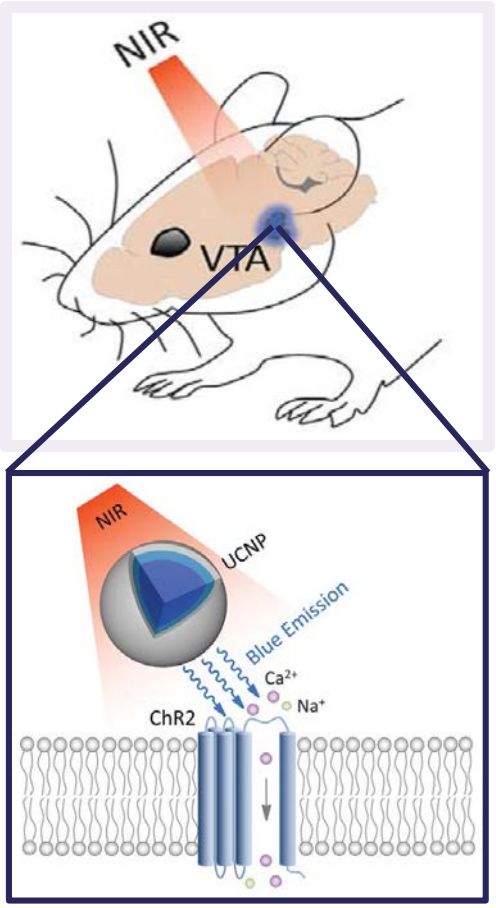
UCNP-mediated optogenetics

→ Successful activation or inhibition of specific neuronal populations (spectral tuning of UCNPs)

→ Successful implementation *in vivo* (biocompatible and long-term stability)

→ Minimally invasive technique to change behaviour

→ Potential in «remote» therapies for neurological disorders



Photon upconversion (UC)

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]

Near-infrared deep brain stimulation via upconversion nanoparticle–mediated optogenetics

Shuo Chen,[1*] Adam Z. Weitemier,[1] Xiao Zeng,[2] Linmeng He,[1] Xiyu Wang,[1] Yanqiu Tao,[1] Arthur J. Y. Huang,[1] Yuki Hashimotodani,[3] Masanobu Kano,[3,4] Hirohide Iwasaki,[5] Laxmi Kumar Parajuli,[5] Shigeo Okabe,[5] Daniel B. Loong Teh,[6] Angelo H. All,[7] Iku Tsutsui-Kimura,[8] Kenji F. Tanaka,[8] Xiaogang Liu,[2,9*] Thomas J. McHugh[1,10*]

Near-infrared light induced *in vivo* photodynamic therapy of cancer based on upconversion nanoparticles

Chao Wang, Huiquan Tao, Liang Cheng, Zhuang Liu*

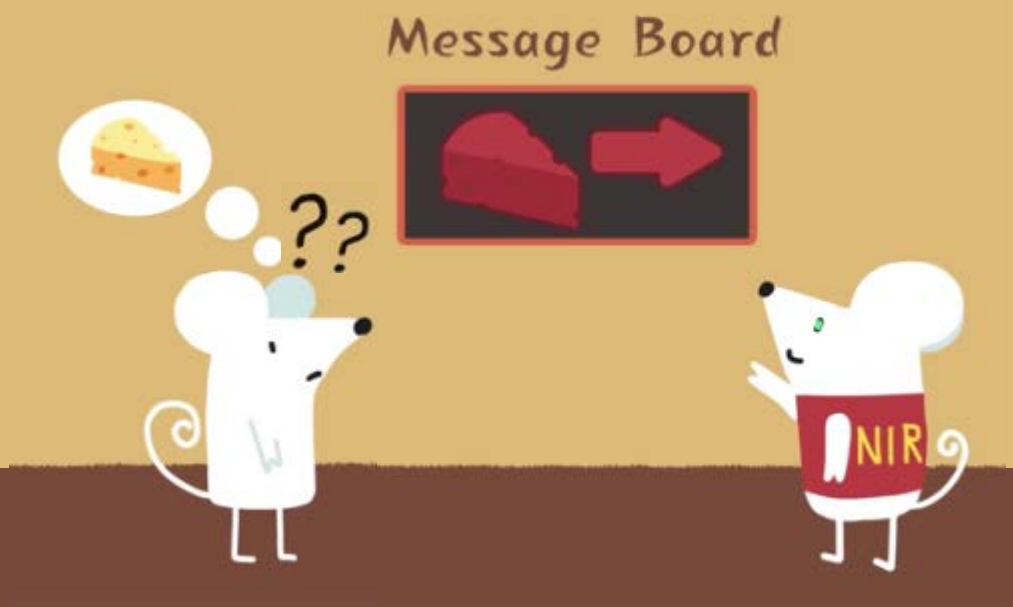
Dual-modality *in vivo* imaging using rare-earth nanocrystals with near-infrared to near-infrared (NIR-to-NIR) upconversion luminescence and magnetic resonance properties

Jing Zhou [a], Yun Sun [a], Xiaoxia Du [b], Liqin Xiong [a], He Hu [a], Fuyou Li [a,*]

Photon upconversion facilitated molecular solar energy storage†

Karl Börjesson,[a] Damir Dzebo,[b] Bo Albinsson[b] and Kasper Moth-Poulsen*[a]

Upconversion Nanoparticles (UCNPs) in Neuroscience



Journal Club, 16th April 2019

Alexandra Bentrup

Yuqian Ma *et al.*, *Cell* (2019); https://doi.org/10.1016/j.cell.2019.01.038