Oculus Reparo

Polymer Nanoparticles for Rescuing Vision in Blind Retinas

Guglielmo Lanzani

Center for Nano Science and Technology

Istituto Italiano di Tecnologia

Dept. of Physics, Politecnico di Milano

Multi disciplinary collaboration

Center for Nano Science and Technology, Istituto Italiano di Tecnologia, Milan, Italy
Maria Rosa Antognazza, Greta Chiaravalli, Daniele Fazzi, Giovanni Manfredi, Sara Perotto. Alumni: Jonathan Barsotti, Sebastiano Bellani, Caterina Bossio, Eleonora Canesi, Andrea Desii, Michele Garbugli, Ester Giussani, Erica Lanzarini, Lucia Laudato, Francesco Lodola, Matteo Porro, Gabriele Tullii, Elena Zucchetti.

Department of Biology - University of Pisa, Italy
José Fernando Maya-Vetencourt

ISMN-ISOF-IMM-CNR Bologna Italy
Giovanna Barbarella, Valentina Benfenati, Francesca Di Maria, Stefano Ferroni, Mattia Zangoli

Innovhub-SSI, Silk Division, 20133 Milan, Italy
Ilaria Donelli, Giuliano Freddi

ISTM-CNR Perugia, Italy
Edoardo Mosconi, Paolo Salvatori, Filippo De Angelis

Istituto Officina dei Materiali CNR-IOM SLACS Cagliari, Cittadella Universitaria, 09042 Monserrato (California), Italy
Maria Ilenia Saba, Alessandro Mattoni

I b]j Yfg]hÙdegli Studi di Milano-Bicocca,Milan, Italy
Sergio Brovelli, Francesco Bruni, Beatriz Santiago Gonzalez

Politecnico di Milano, Italy
Chiara Bertarelli, Cosimo D'Andrea, Francesco Scotognella

Center for Synaptic Neuroscience and Technology, Istituto Italiano di Tecnologia, Genoa, Italy
Fabio Benfenati, Elisabetta Colombo, Mattia Difrancesco, Stefano Di Marco, Ermanno D. Papaleo, Cyril Eleftheriou, Giulia Mantero, Mattia Nova, Anna Rocchi, Dmytro Shmal. Alumni: Mattia Bramini, Marco Dal Maschio, Paul Feyen, Diego Ghezzi,

Department of Biotechnology and Applied Clinical Science, University of L'Aquila, Italy.
Silvia Bisti, Mattia Di Paolo, Rita Maccarone

Department of Health Science, Nuclear Medicine, University of Genoa, 16132 Genoa, Italy
Ambra Buschiazzo, Vanessa Cossu, Gianmario Sambuceti, Flavia Ticconi

Animal Facility, National Institute Cancer Research, IRCCS AOU San Martino-IST, 16132 Genoa, Italy
Michele Cilli, Laura Emionite

IBFM-CNR, Milan, Italy
Cecilia Marini

Ospedale Sacro Cuore – Don Calabria (Verona), Italy
Maurizio Mete, Angela Russo, **Grazia Pertile**

Georgia Institute of Technology, Atlanta, Georgia United States
Jean-Luc 6fÝdas,Hong Li

ISASI-CNR, Naple, Italy
Angela Tino, Claudia Tortiglione

Università degli Studi di Bari "Aldo Moro"
Dr. R. Ragni, Dr. D. Vona, Dr. E. Altamura, Prof. G. M. Farinola

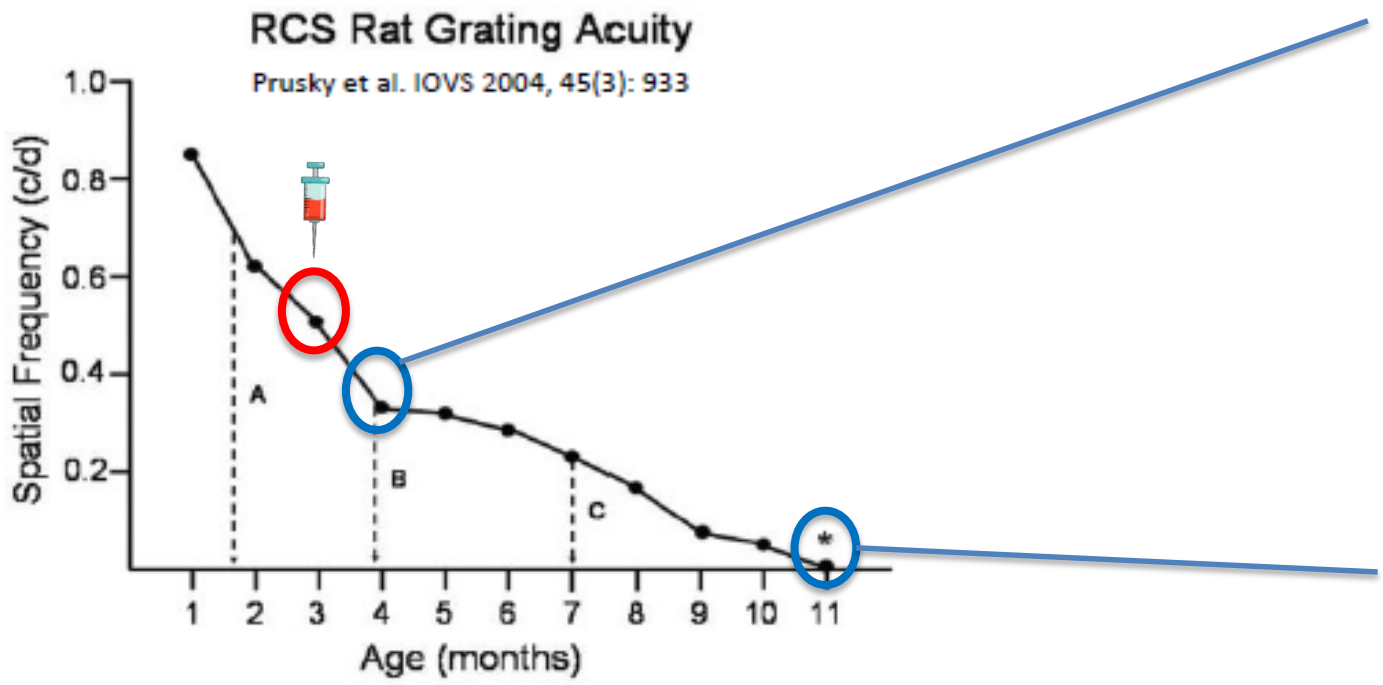
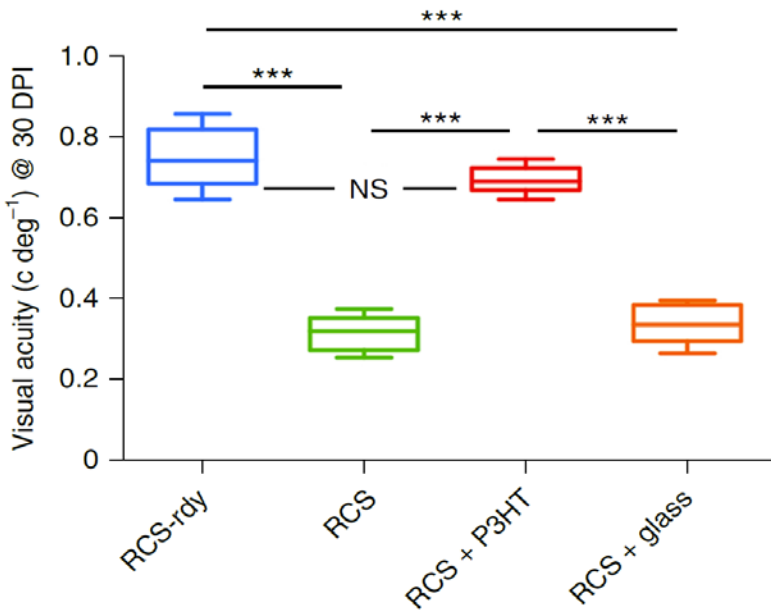
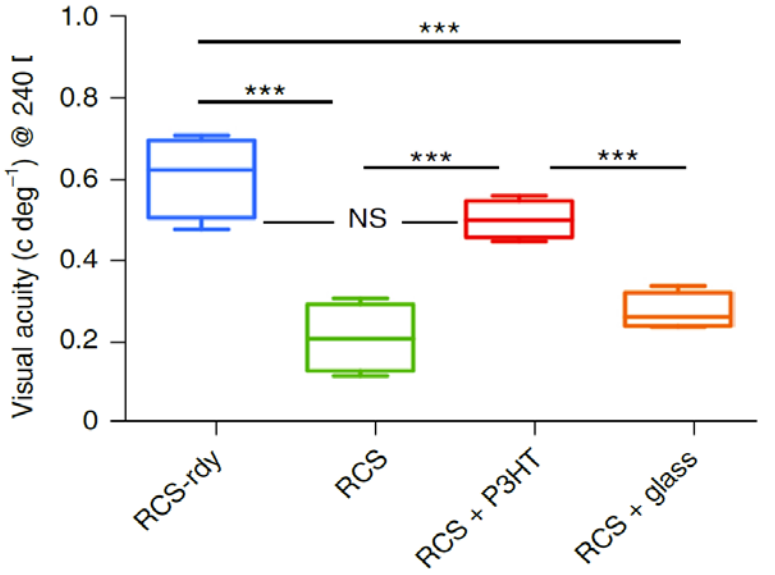


FIGURE 2. RCS rat grating acuity as a function of age. There was a rapid decrease in the grating acuity until 4 months of age. A slower decline in acuity then occurred until blindness at 11 months. *Point at which the animal could not determine a black computer screen from a white one.





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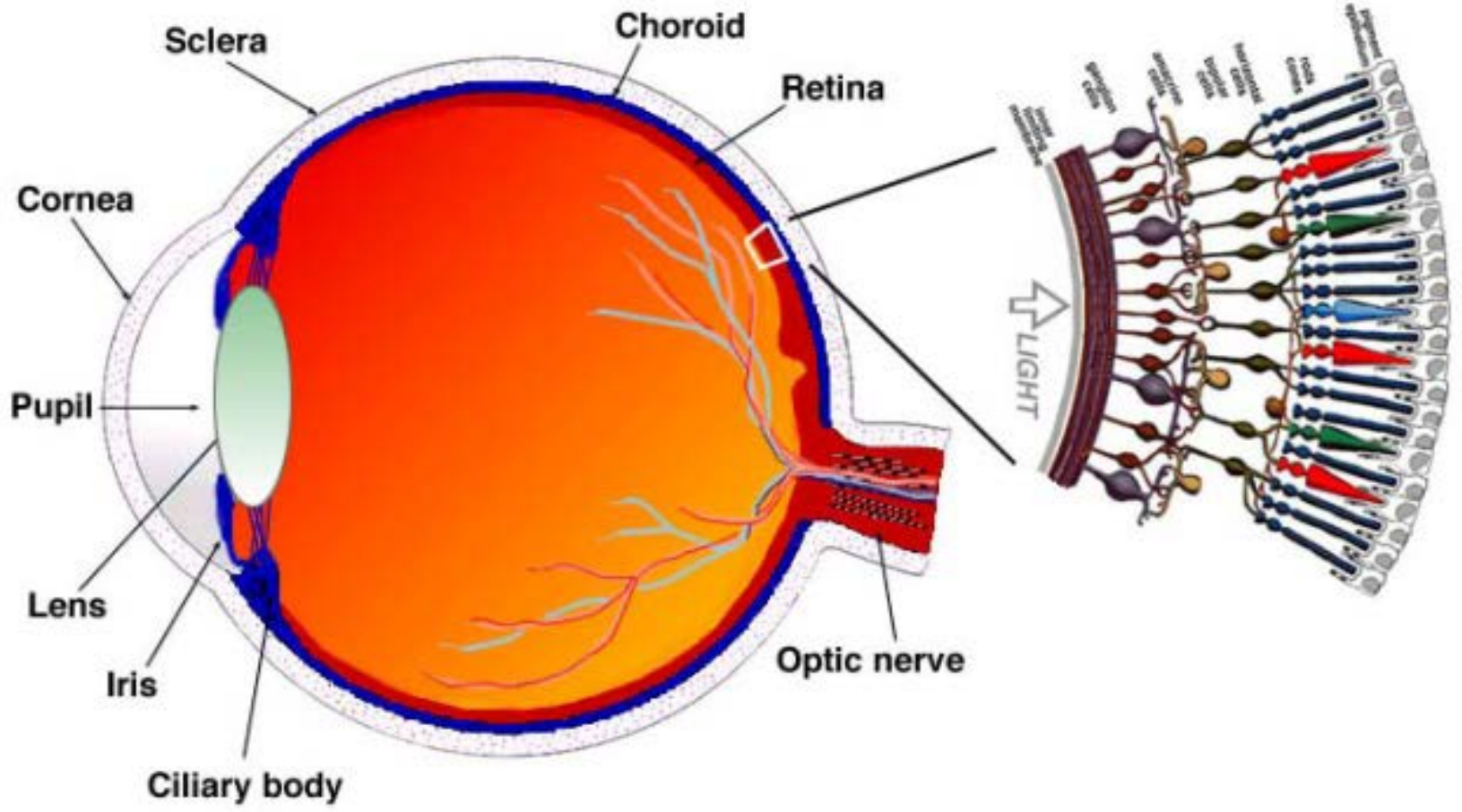
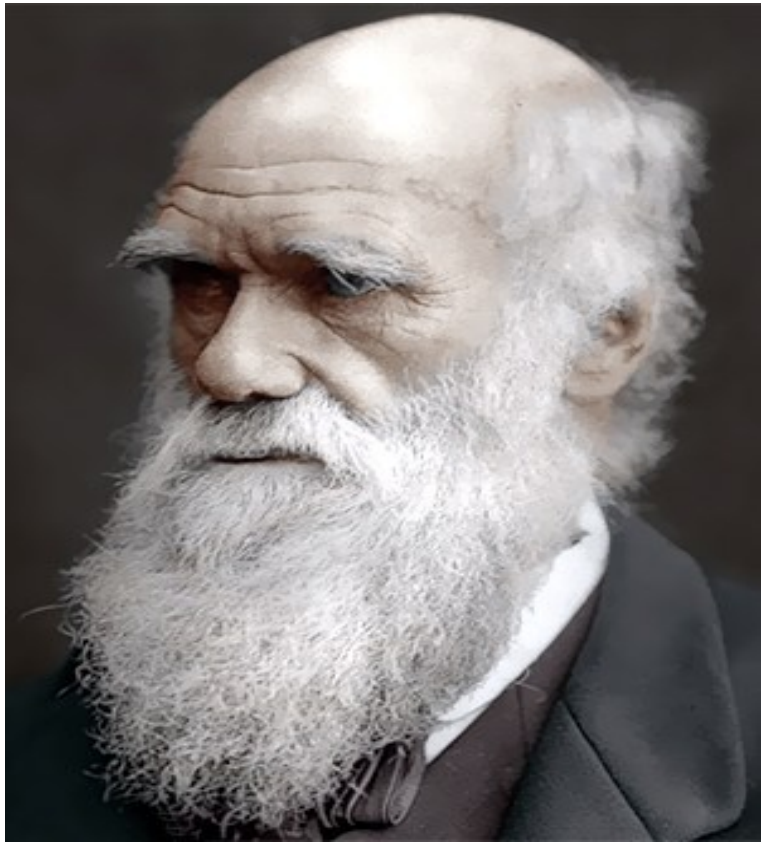
OUTLINE

- Motivation
- Retina Prosthesis
- P3HT and Nanoparticles Photophysics
- Optostimulation mechanism

Il più sofisticato organo di senso

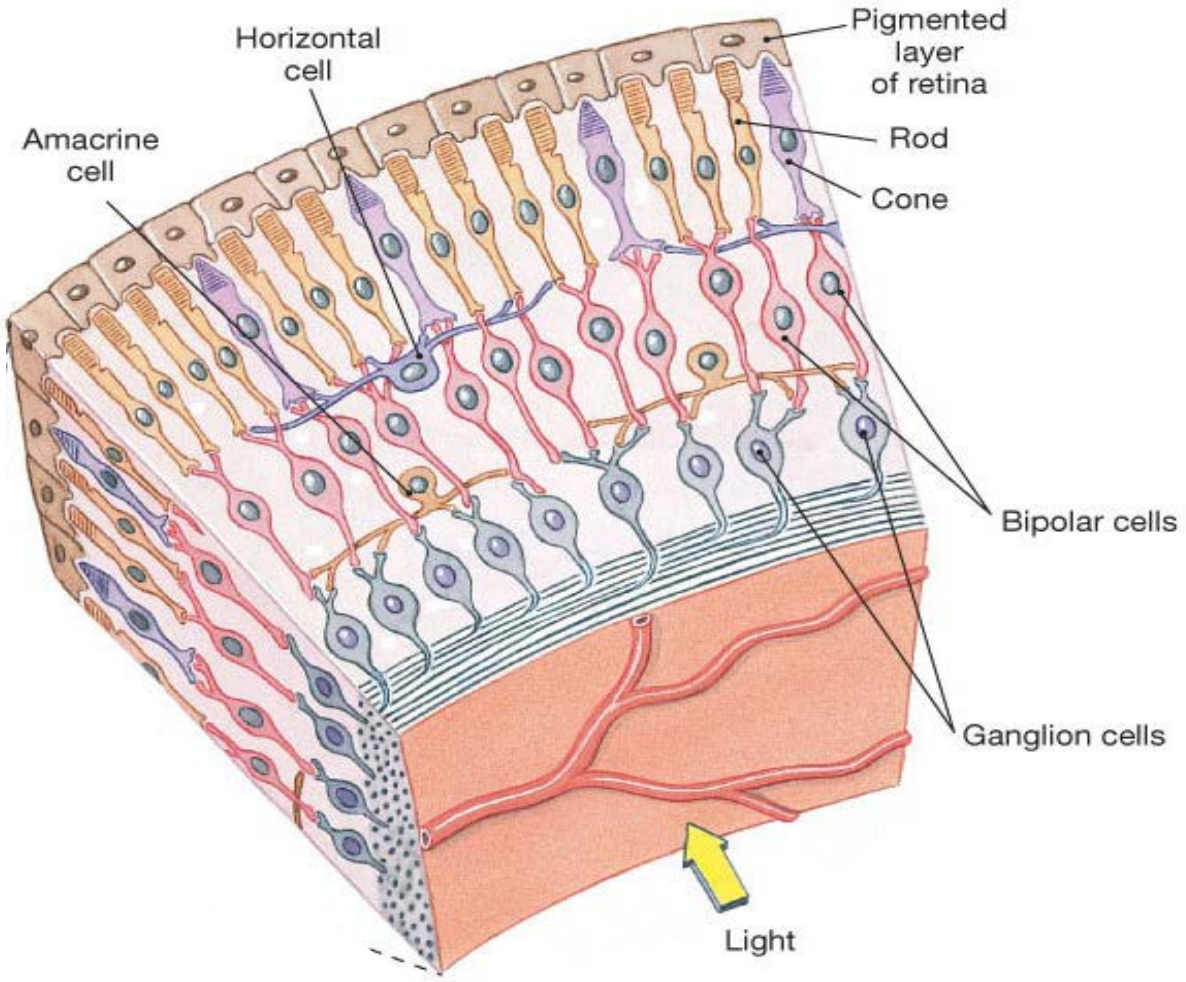




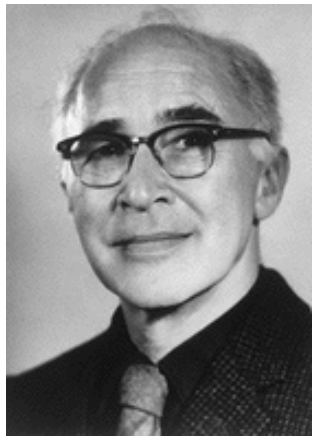
Charles Darwin

“To suppose that the eye, with all its inimitable contrivances for adjusting the focus to different distances, for admitting different amounts of light, and for the correction of spherical and chromatic aberration, could have been formed by natural selection, seems, I freely confess, absurd in the highest possible degree.”

The Retina

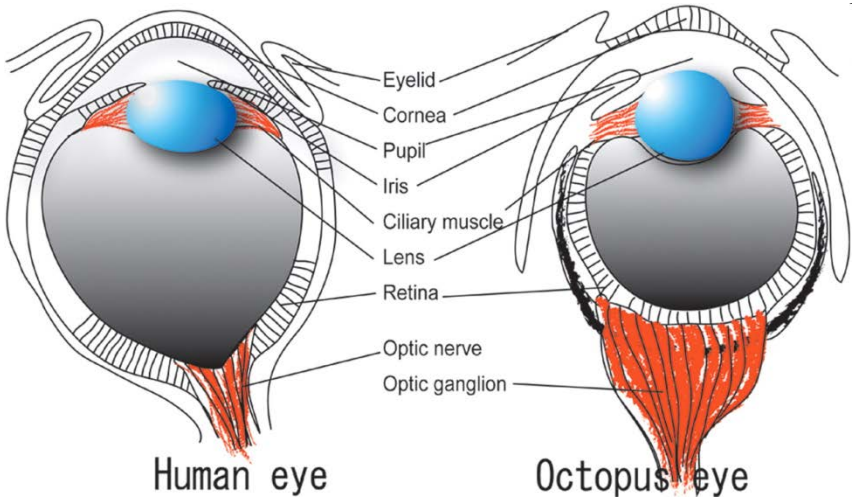

Horizontal cell
Pigmented layer of retina
Amacrine cell
Rod
Cone
Bipolar cells
Ganglion cells
Light

Evolution Strategy



George Wald

blood vessel-free



Octopus

Great salad

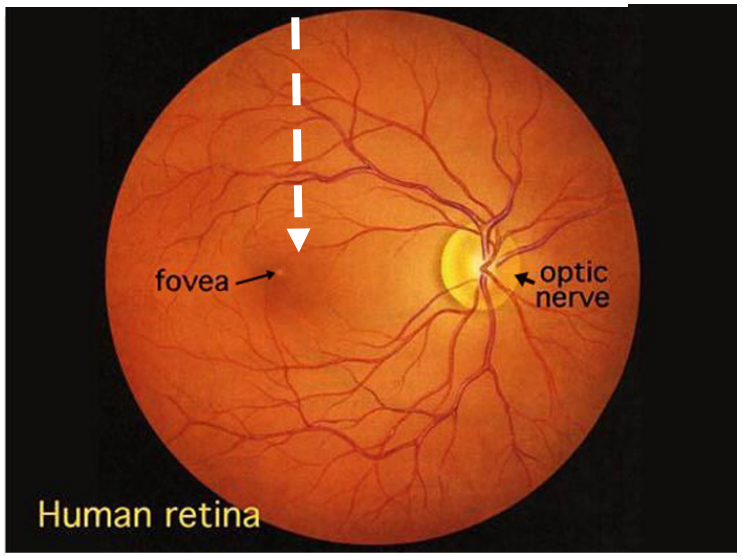
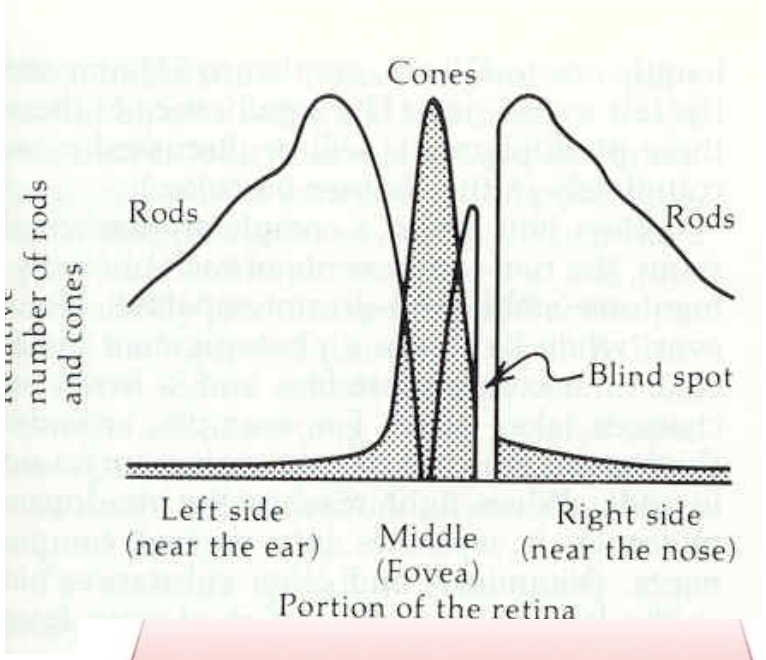


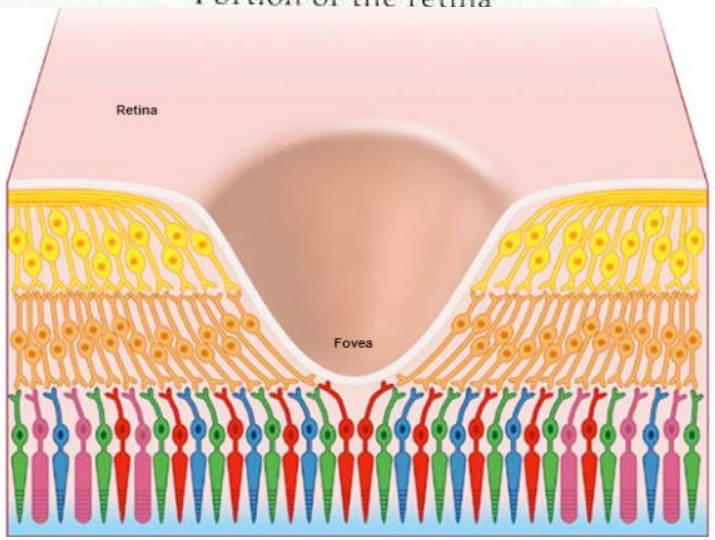
Fig. 1. Human retina as seen through an opthalmoscope.

1 mm

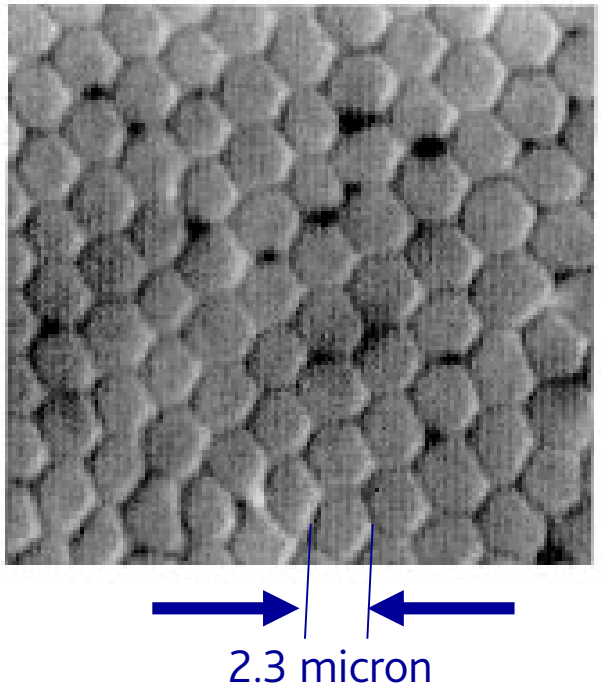
The Blind Spot

Distribuzione spaziale dei fotorecettori

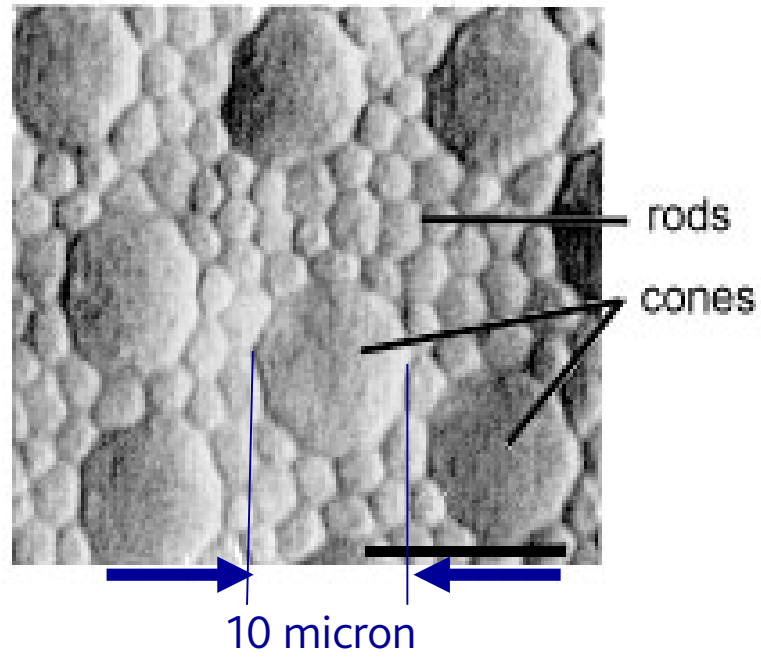




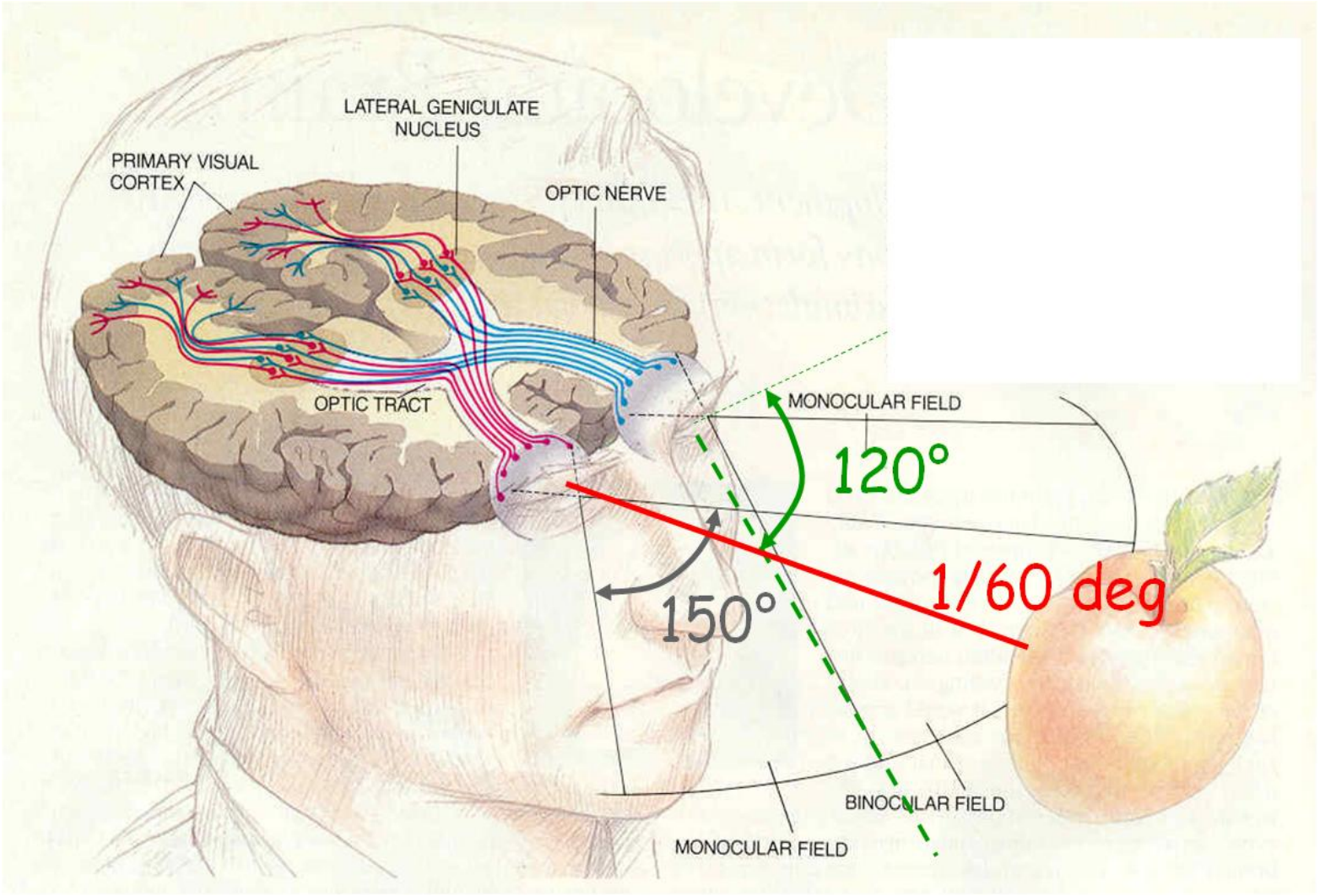
fovea



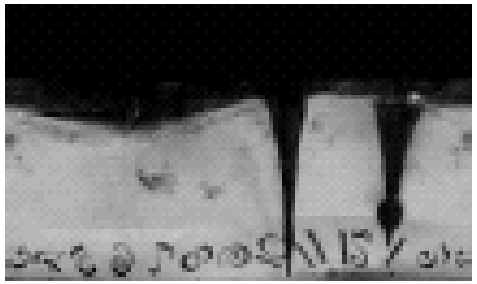
periphery



A broad field of view



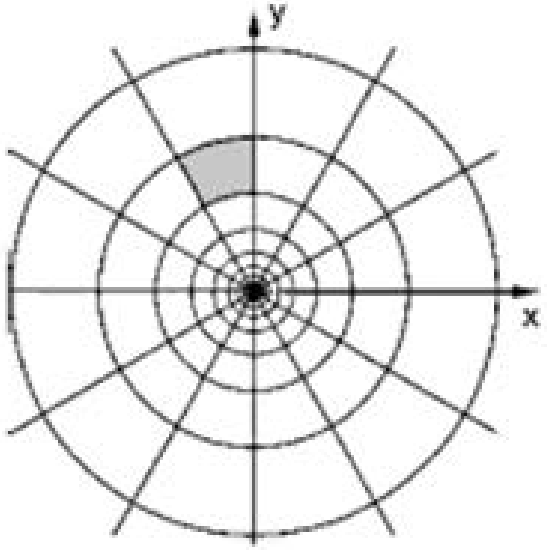
How the brain perceives the world

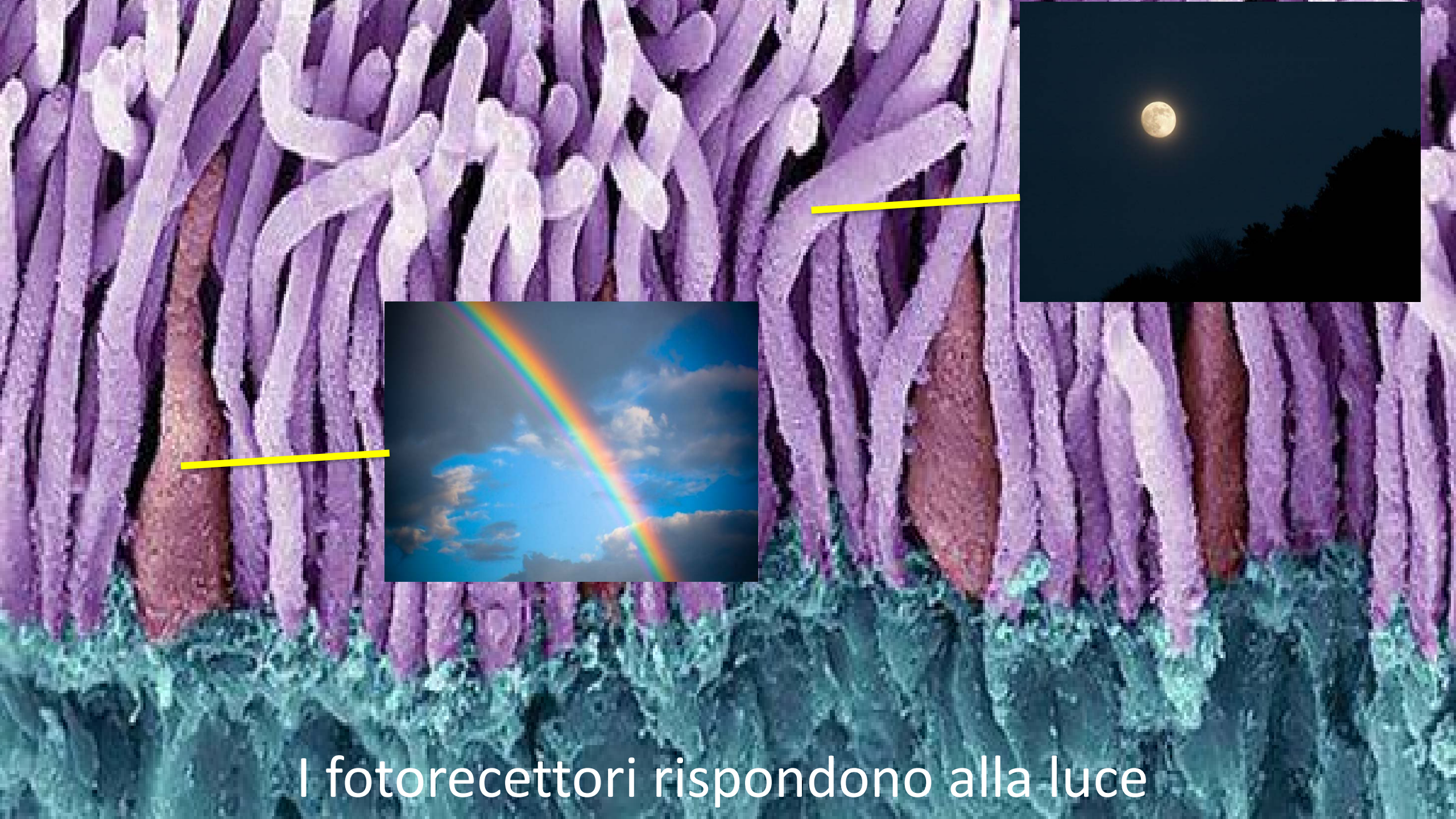


(a)

⇔

(b)





I fotorecettori rispondono alla luce


Peacock Mantis

Neil Harbisson | TEDGlobal 2012

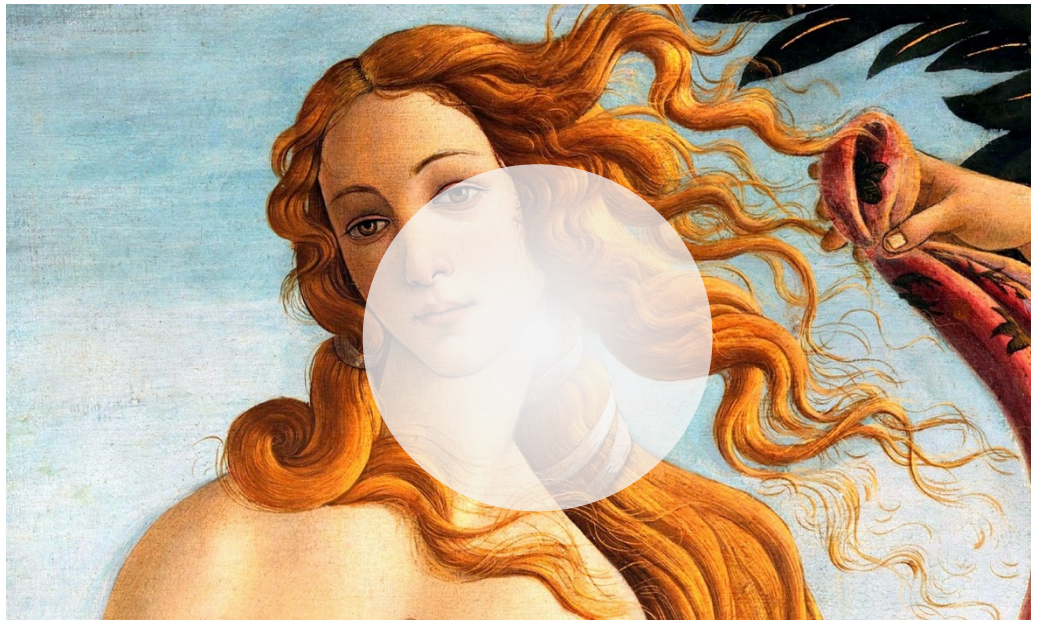
I listen to color

Age-related **macular degeneration** (AMD)

Third among **the global** causes of visual impairment with a blindness prevalence of 8,7%.

The World Health Organization assesses that 50 million persons suffer from AMD symptoms and 14 million persons are blind or severely visually impaired because of AMD.

It is the primary cause of visual deficiency in industrialized countries.



Retinitis Pigmentosa

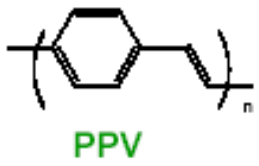
Early Symptoms:
Decreased night vision, loss of peripheral (side) vision

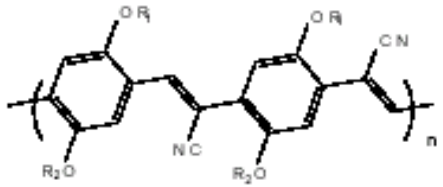
Late Symptoms:
Vision loss, blindness

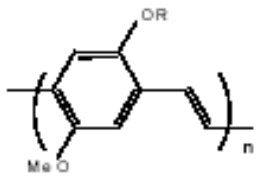
Inherited disease

1 in 3-4000 people
1,5 M people worldwide

Organic Semiconductors

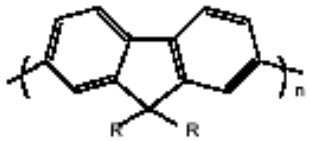

PPV

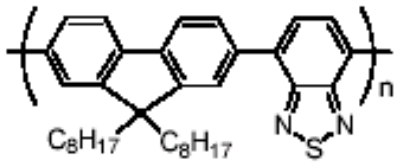

Cyano-PPV

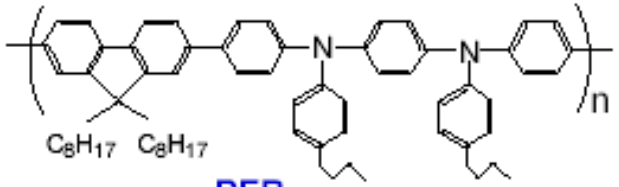

MEH-PPV R = $CH_2CH(Et)Bu$

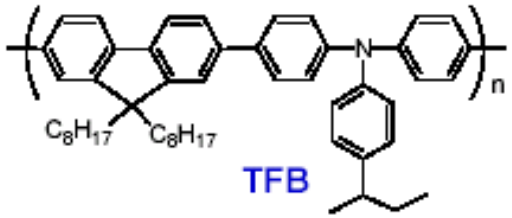
OC_1C_{10} PPV

R = $(CH_2)_3CH(Me)(CH_2)_2CHMe_2$

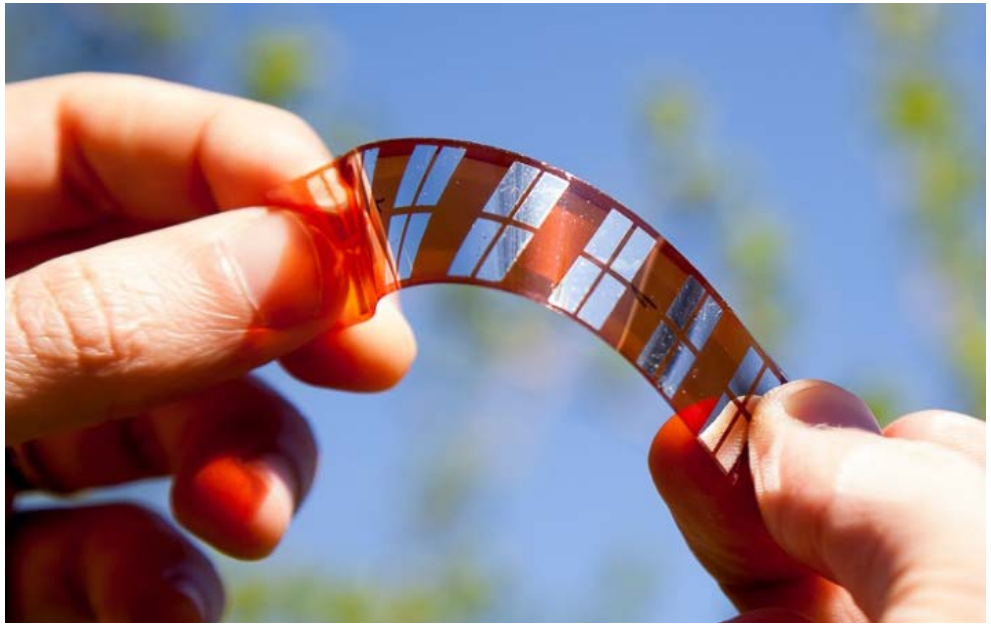

Polyfluorene

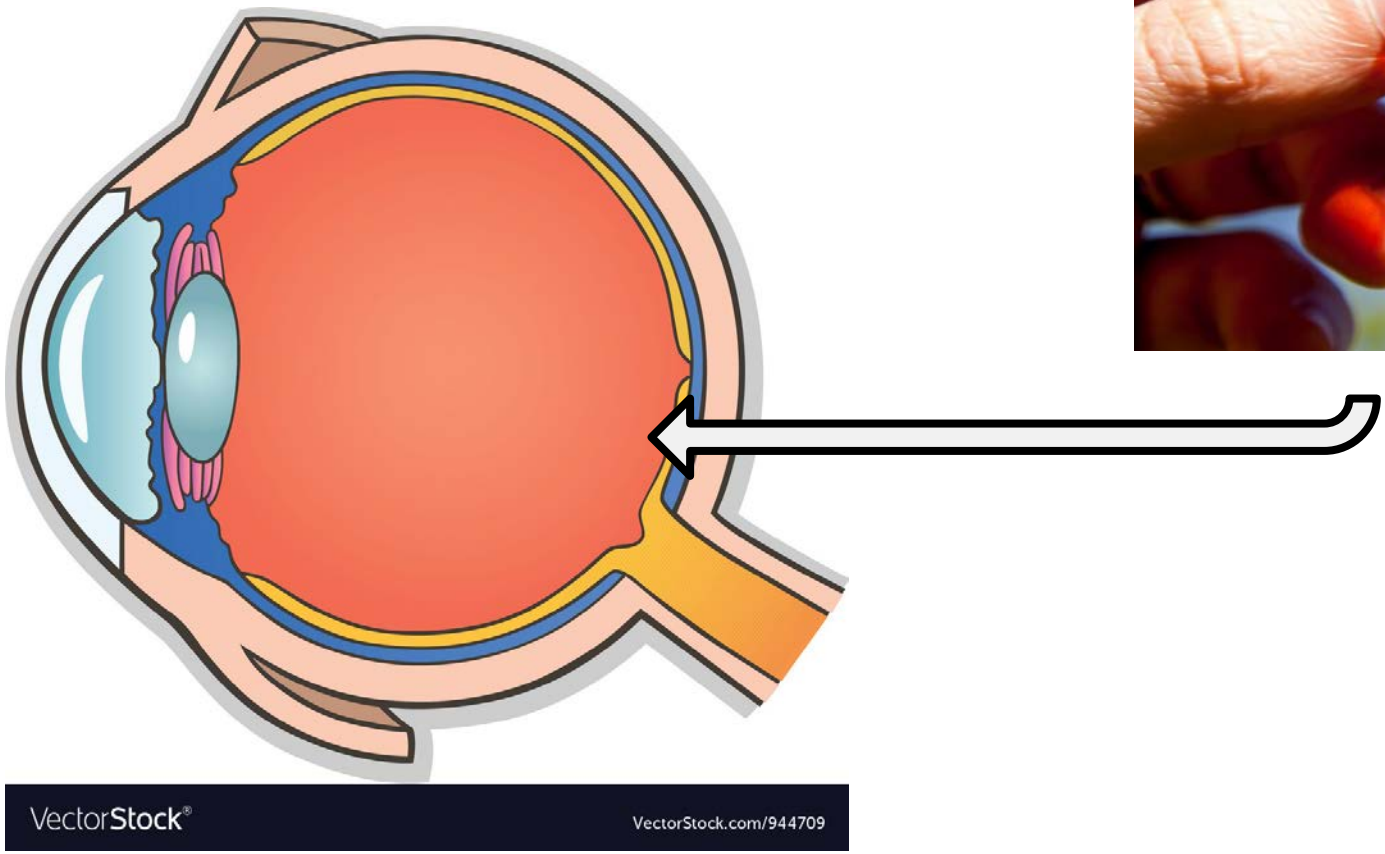

F8BT


PFB


TFB

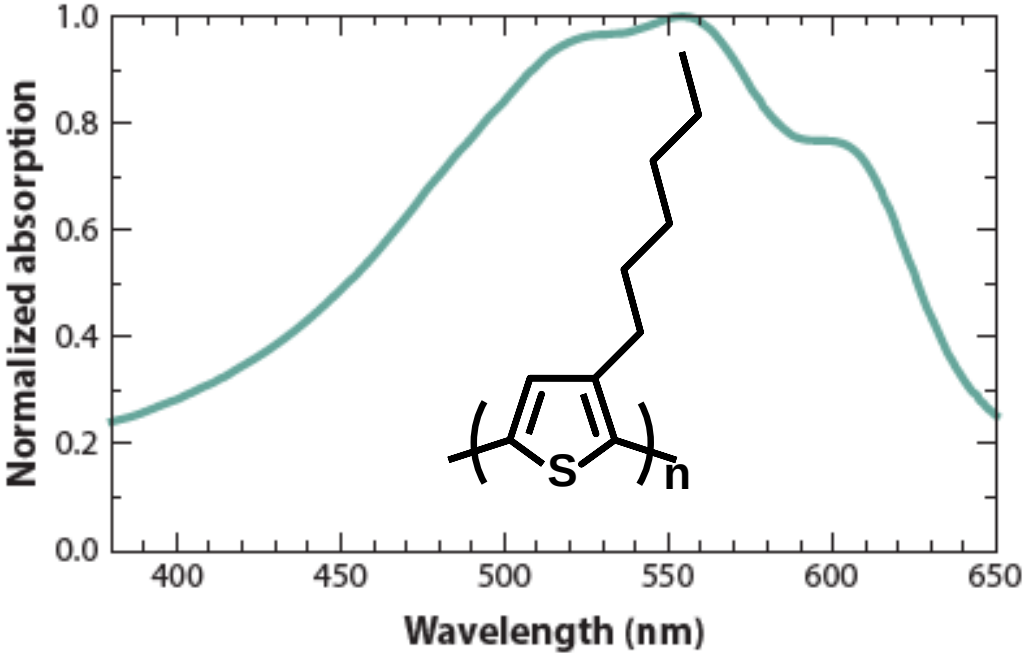
IDEA



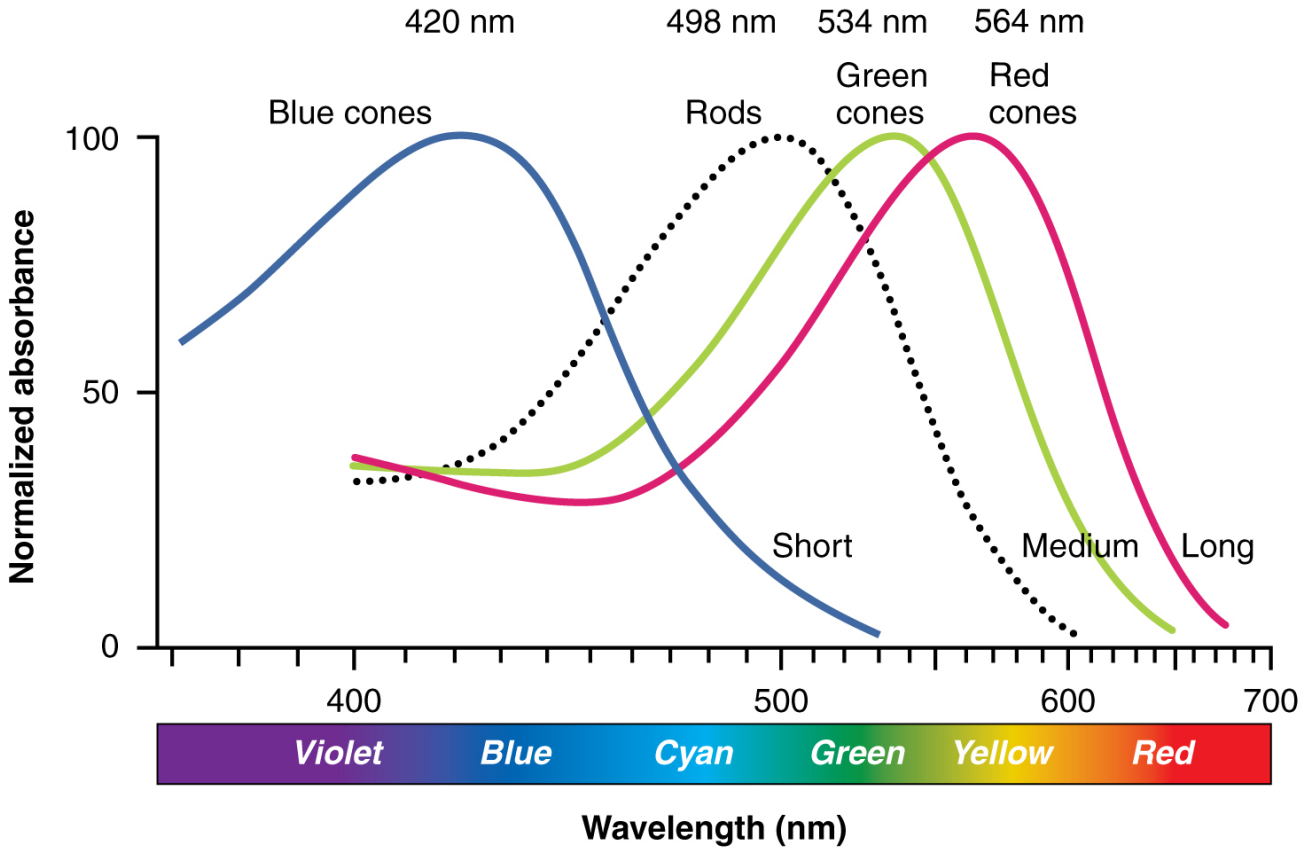


Spectral Response

Poly 3 *hexhyl* Thiophene



Rods and Cones



- Motivation
- Retina Prosthesis
- P3HT and Nanoparticles Photophysics
- Optostimulation mechanism

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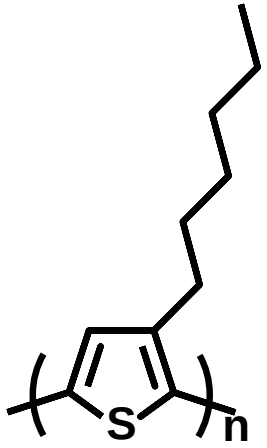
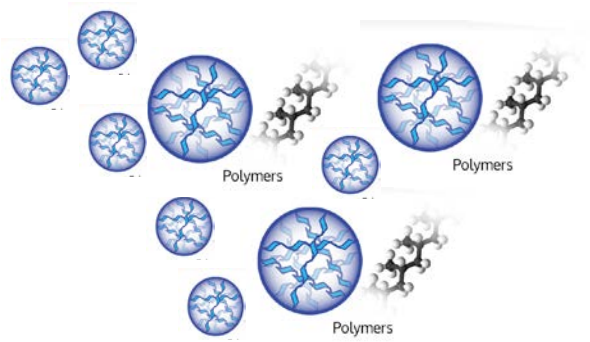
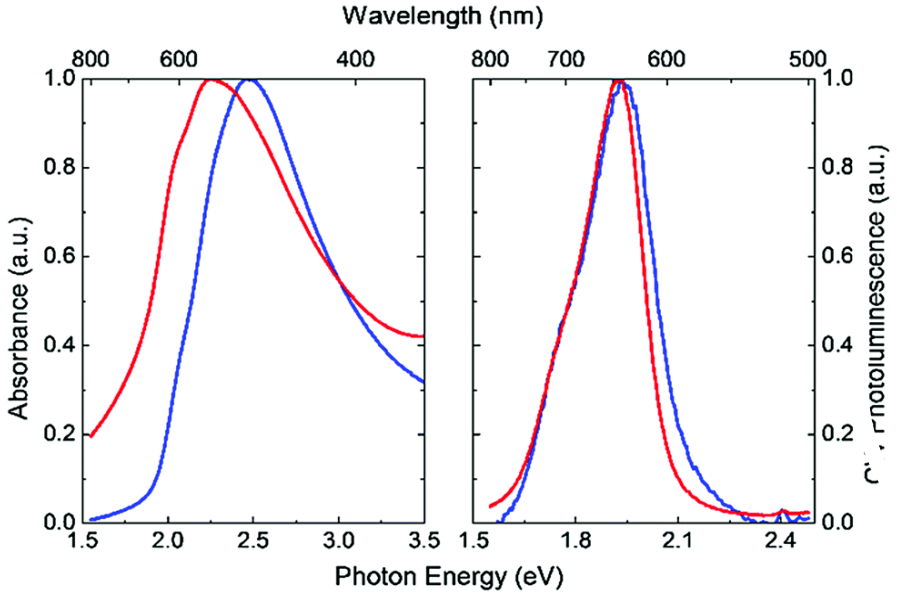
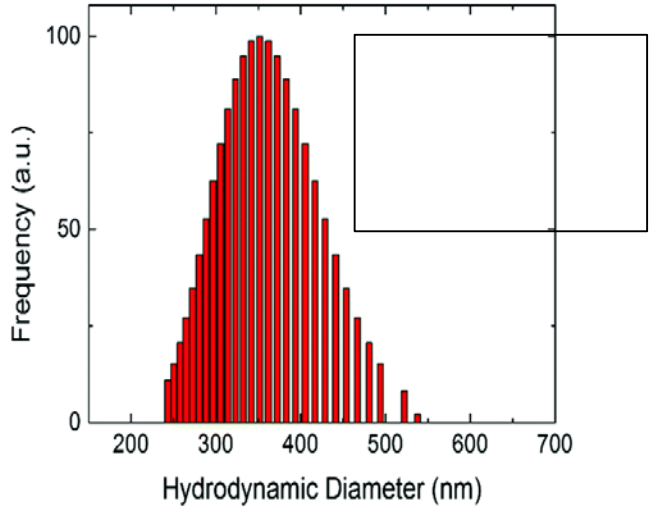
P3HT nanoparticles



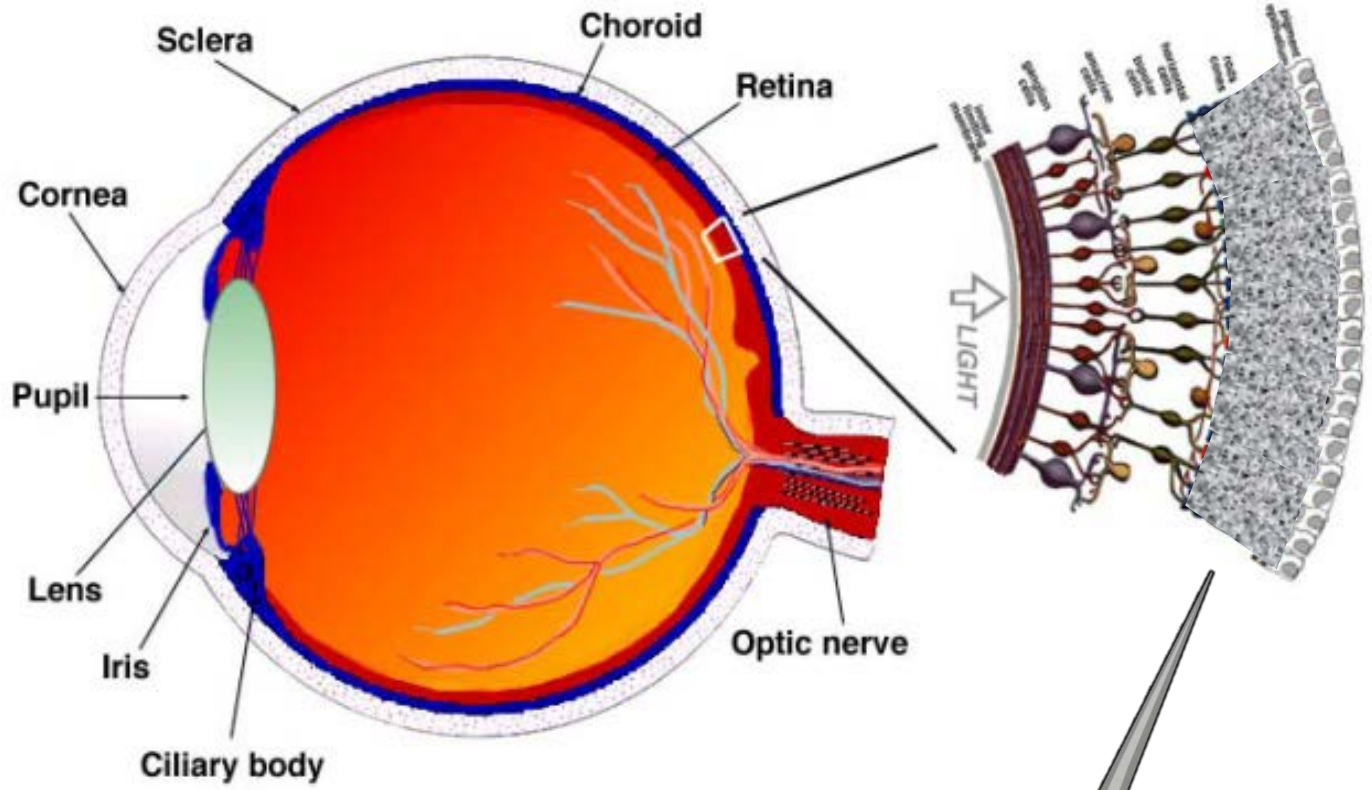


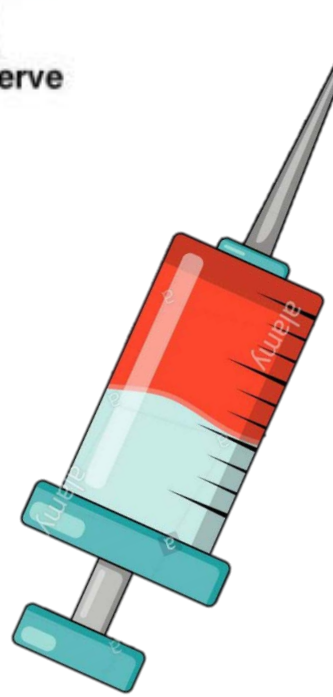
P3HT NANOPARTICLES





Chem. Soc. Rev., 2018 10.1039/C7CS00860K





F. Benfenati

Maurizio Mete

Grazia Pertile

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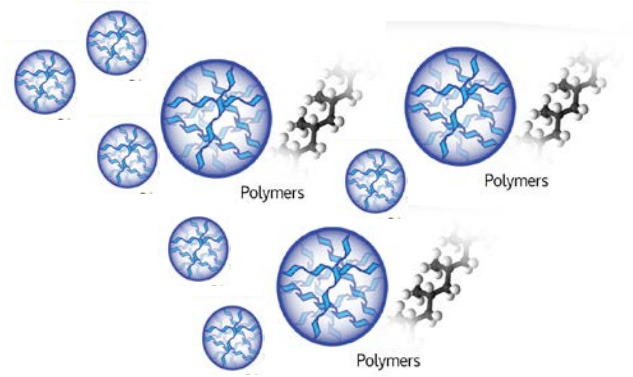
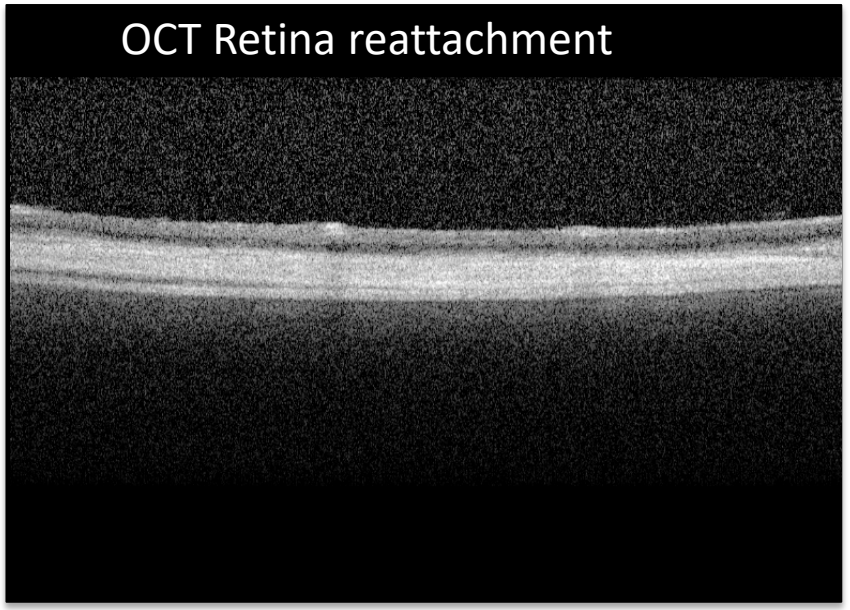
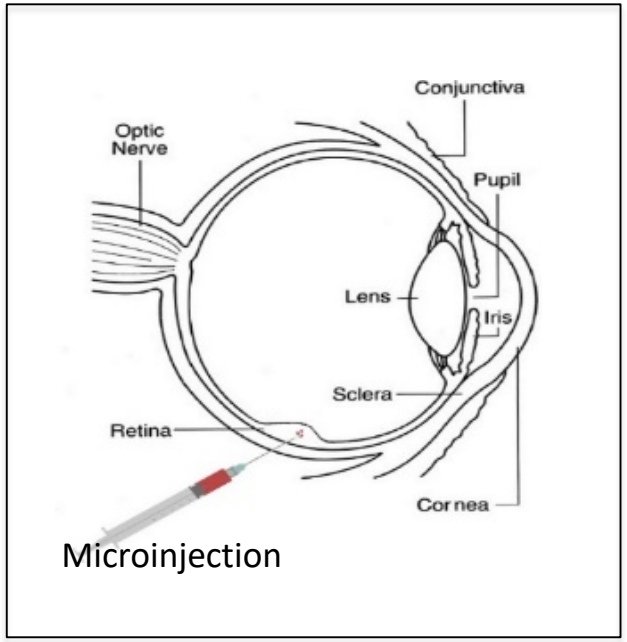
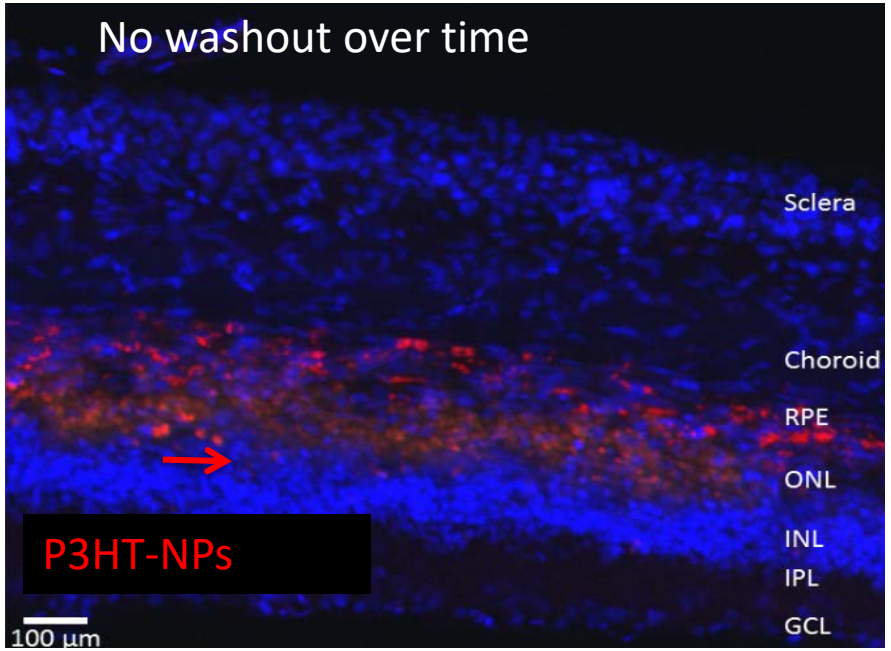
Nanoparticles in retina

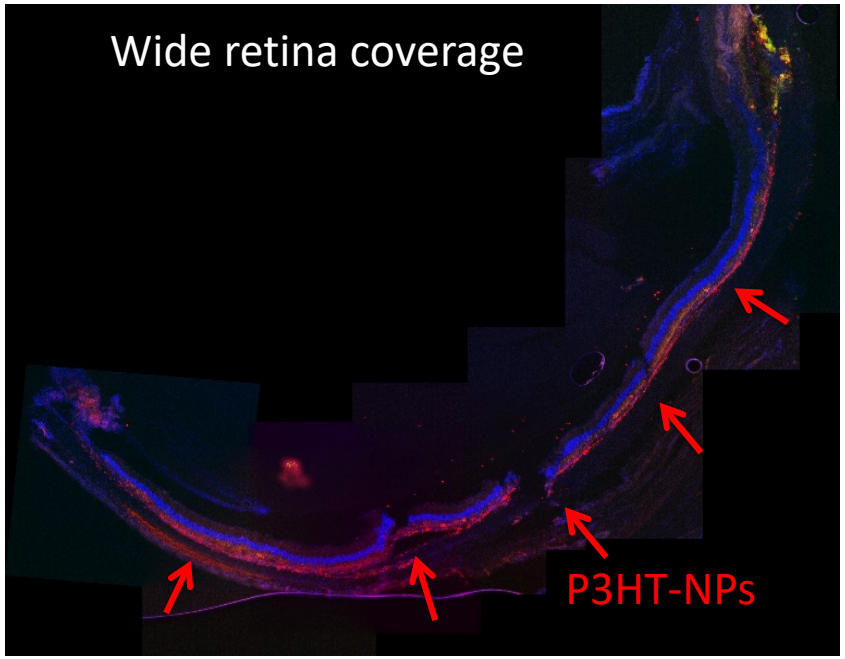
Nature Nanotechnology 15 (8), 698-708 (2020)







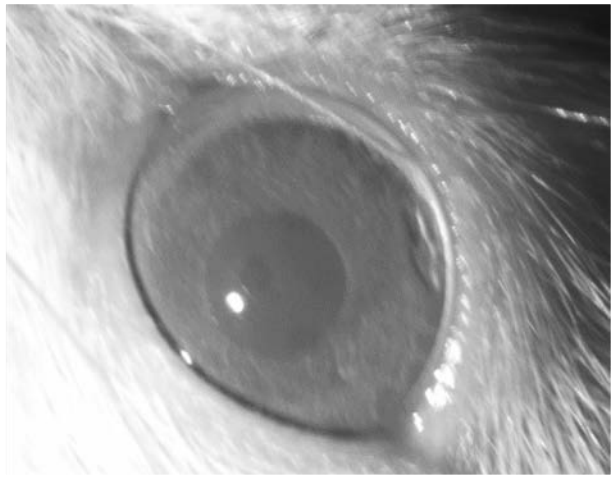




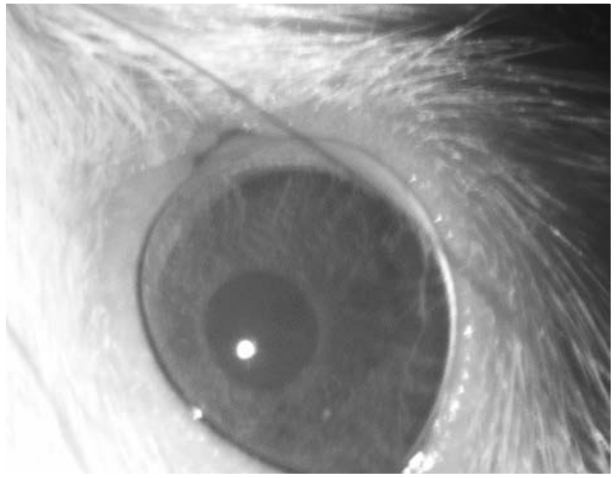
Rescue of pupillary reflex in RCS rats subretinally microinjected with in P3HT-NPs

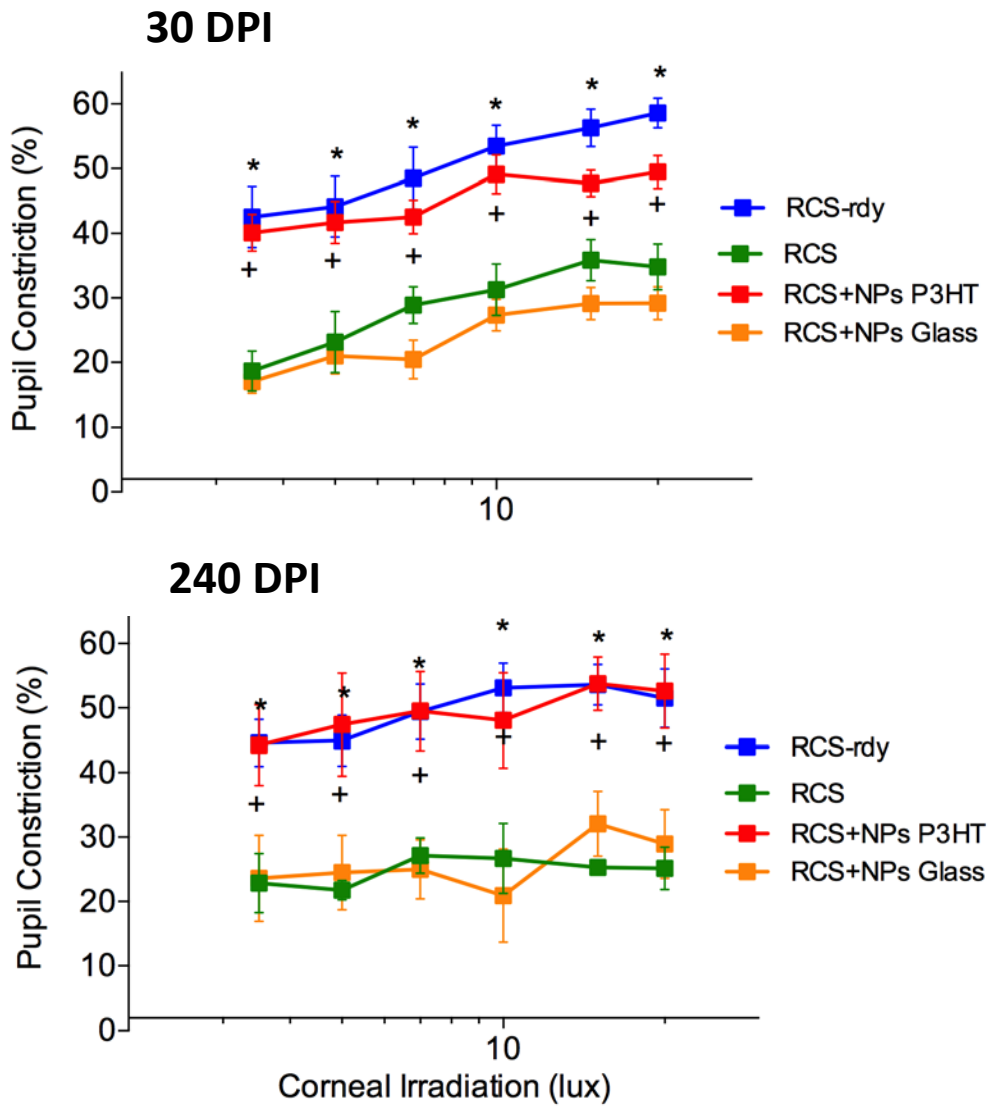
Nature Nanotechnology 15 (8), 698-708 (2020)

Pre



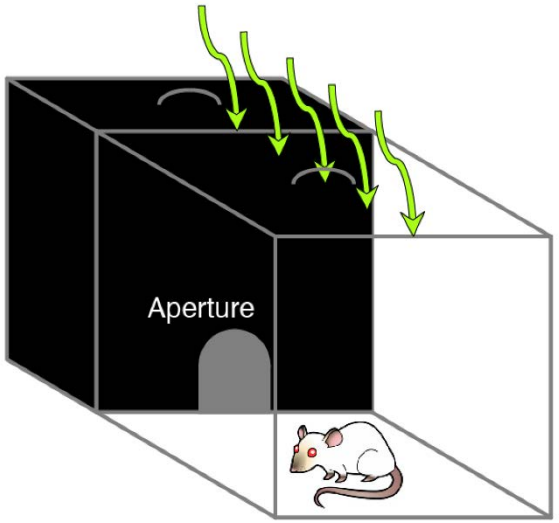
Post



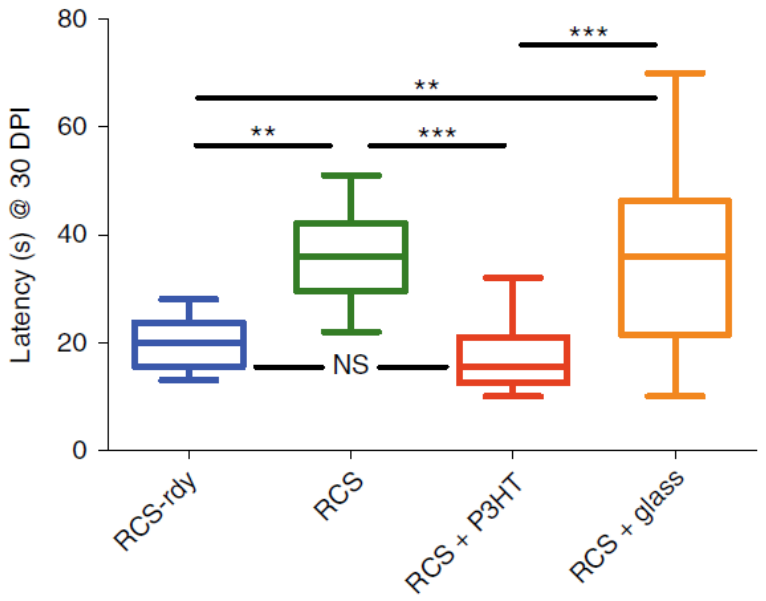


Rescue of visually driven behavior in RCS rats subretinally microinjected with in P3HT-NPs

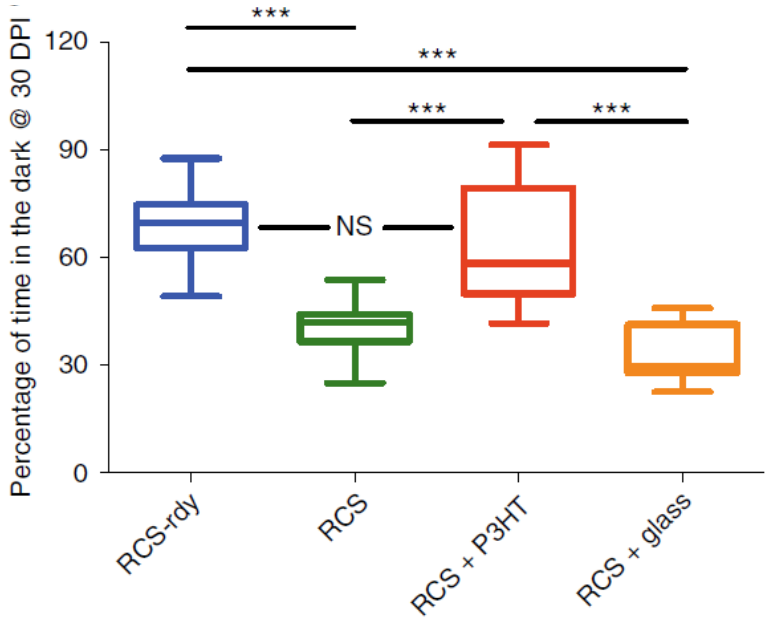
Light-Dark Test (5 lux)

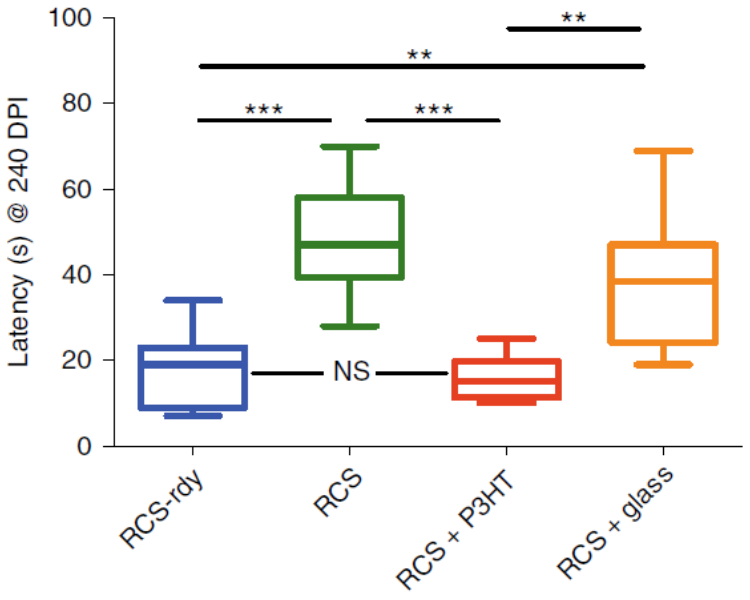


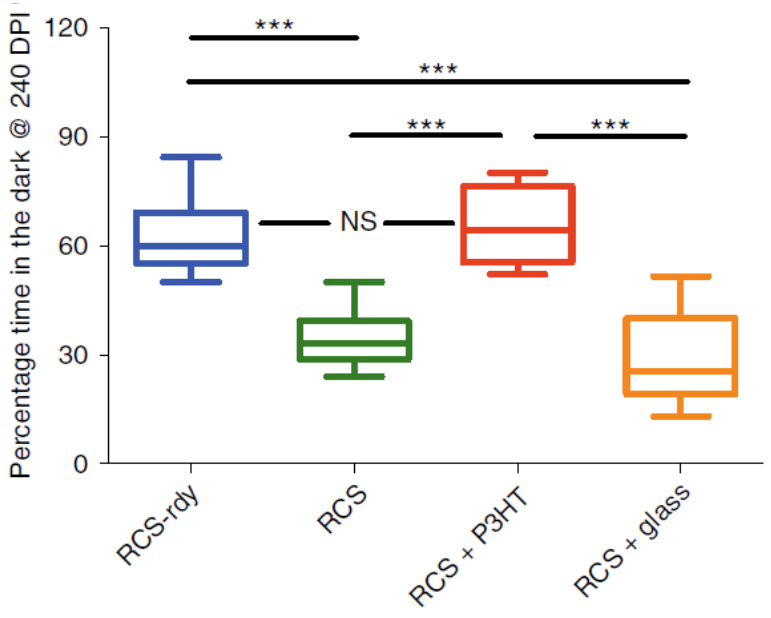
Escape Latency



Time Spent in the Dark

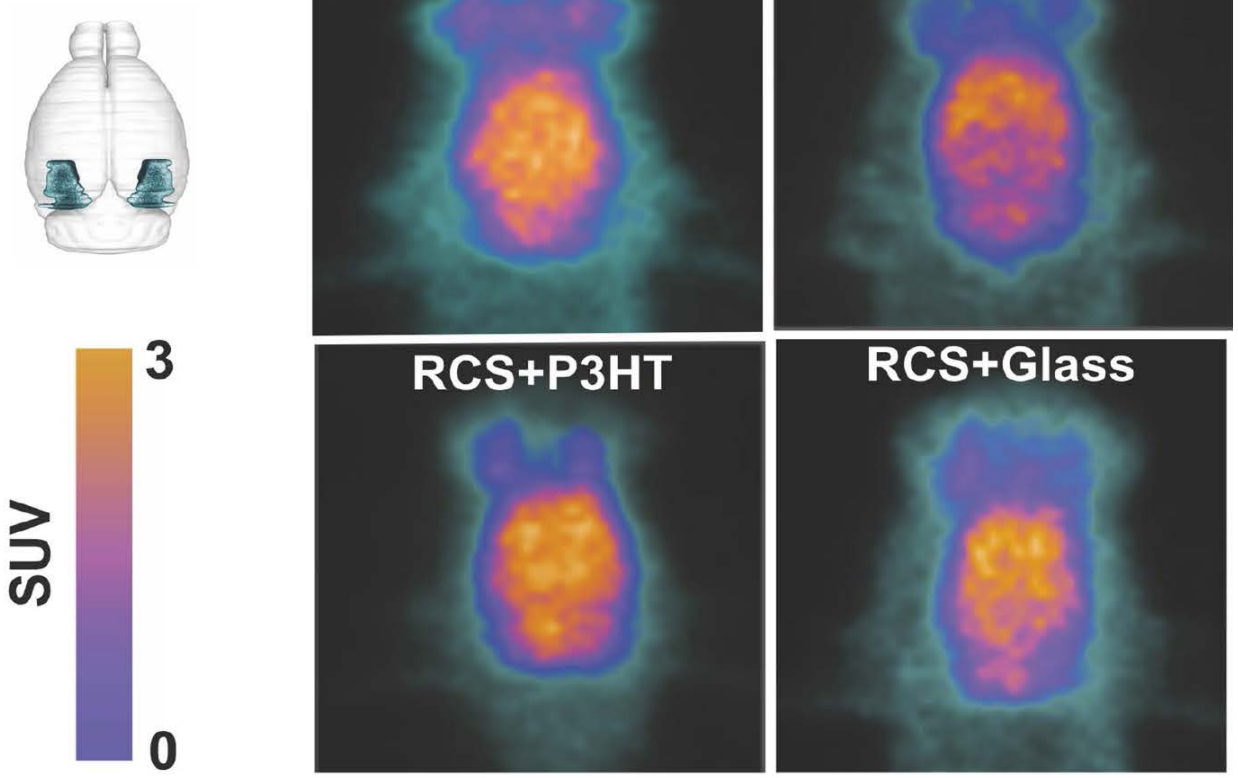




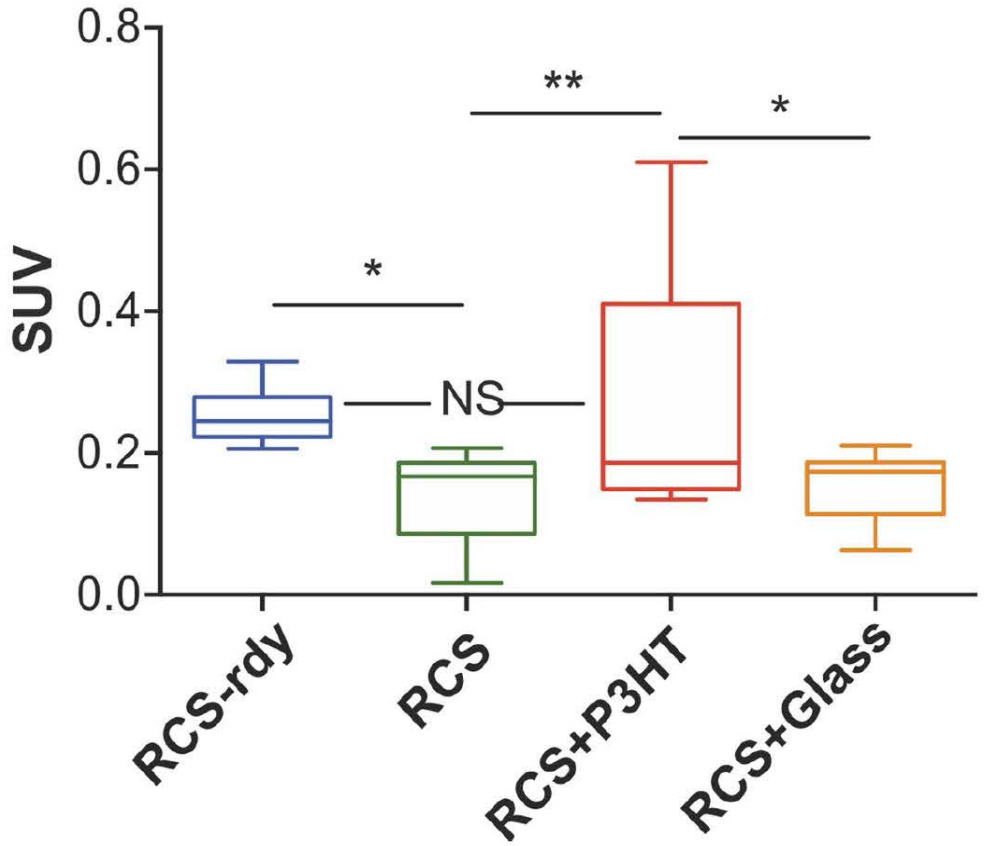


Nature Nanotechnology 15, 698 (2020)

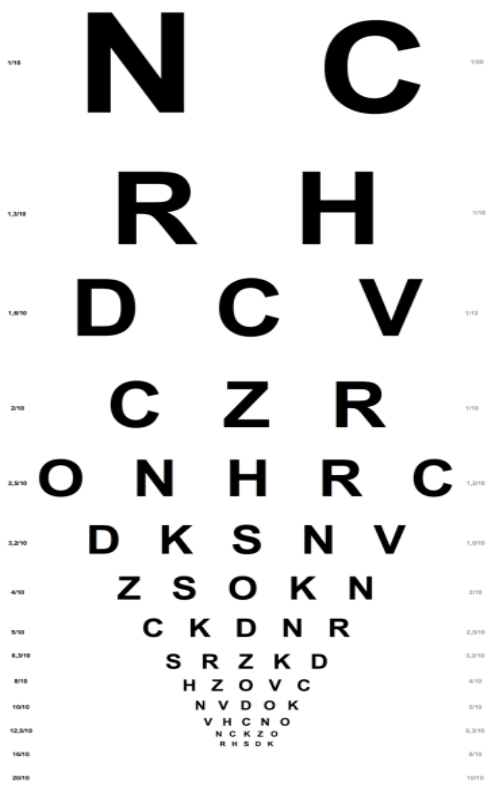
Light-evoked metabolic activation of V1 is rescued in dystrophic RCS rats injected with P3HT nanoparticles

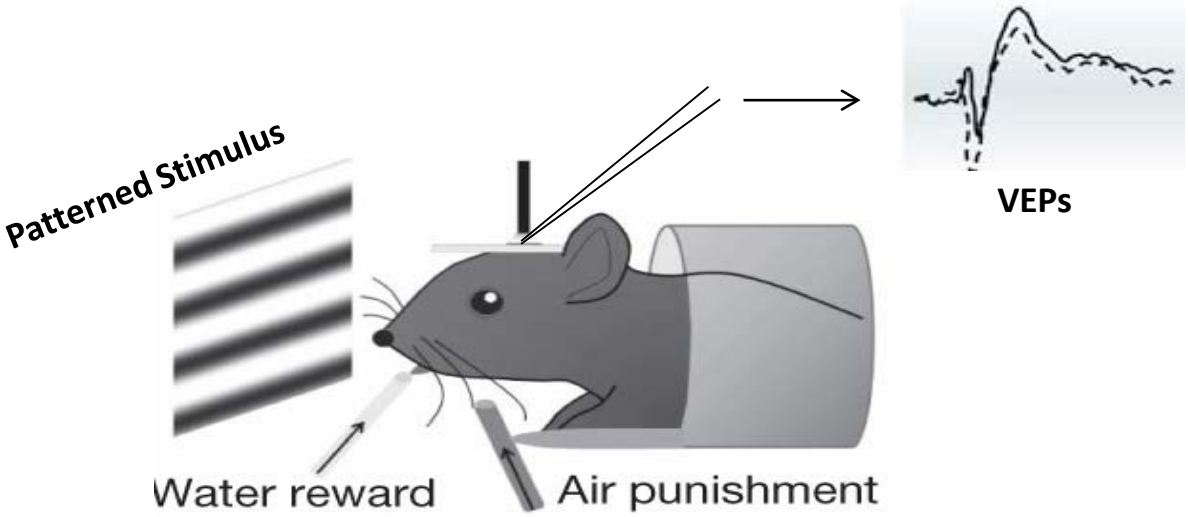


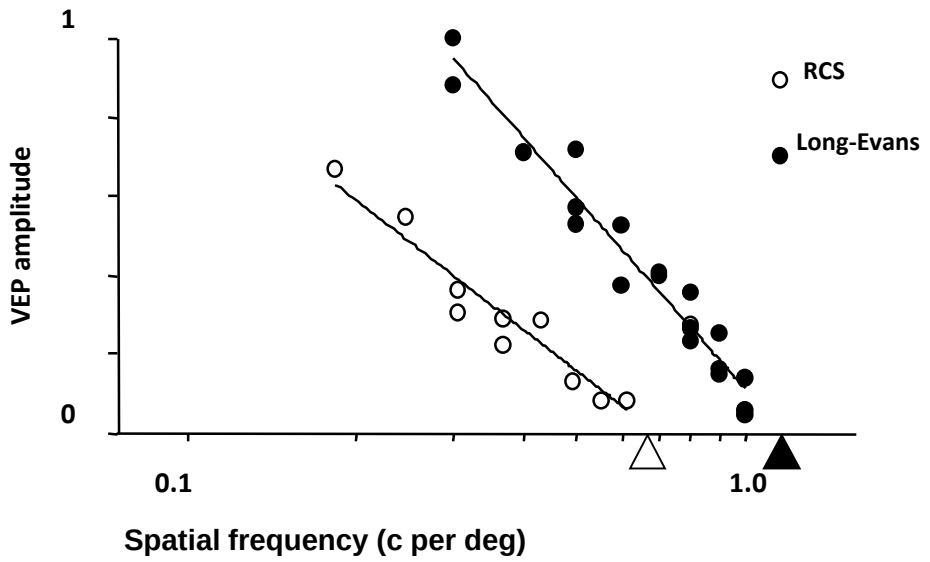
240 DPI



How to measure visual acuity ?

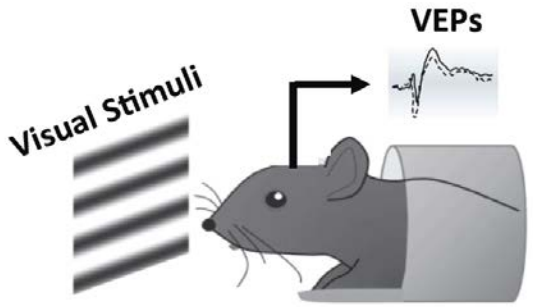


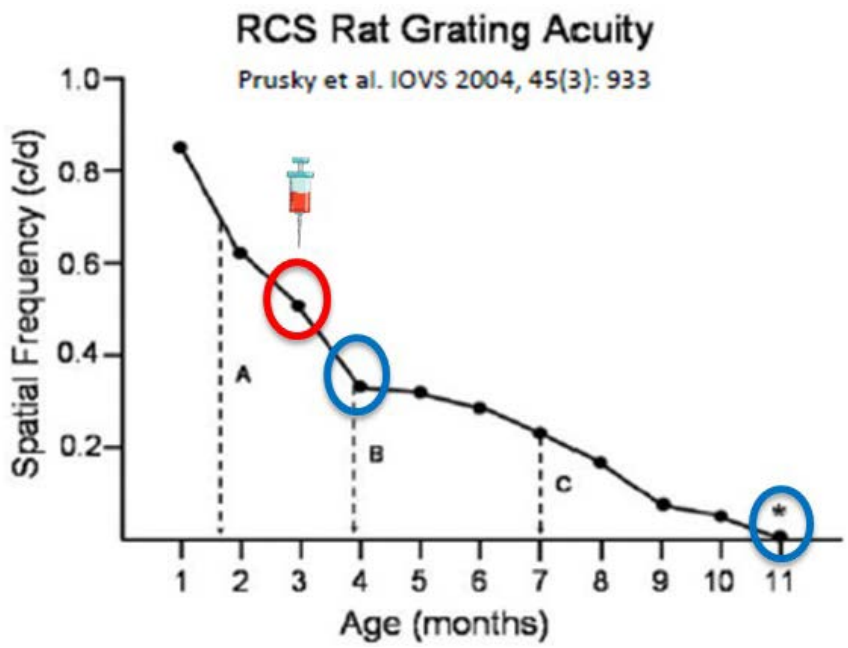


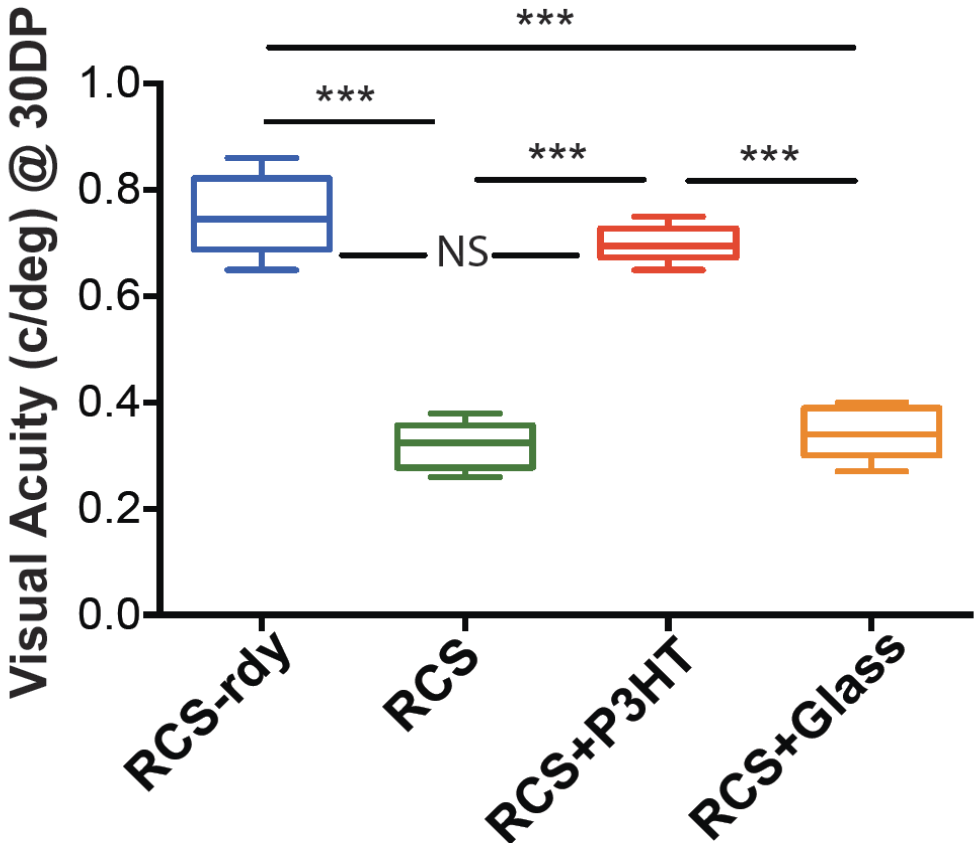


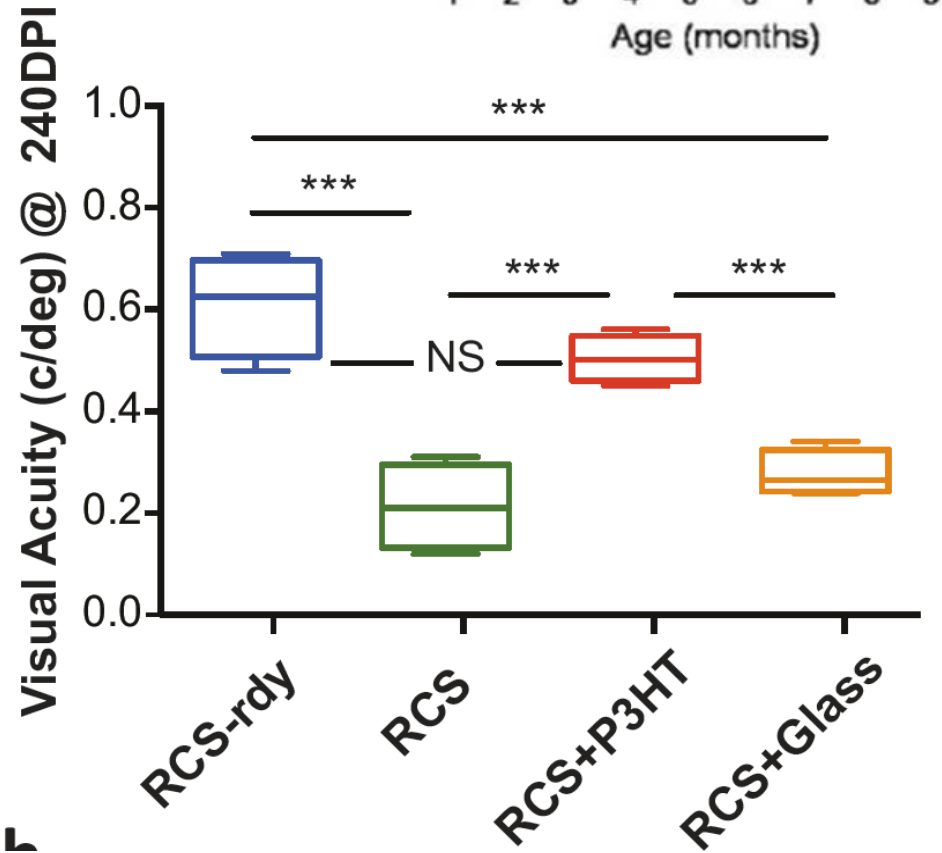
Nature Nanotech 15 (8), 698-708 (2020)

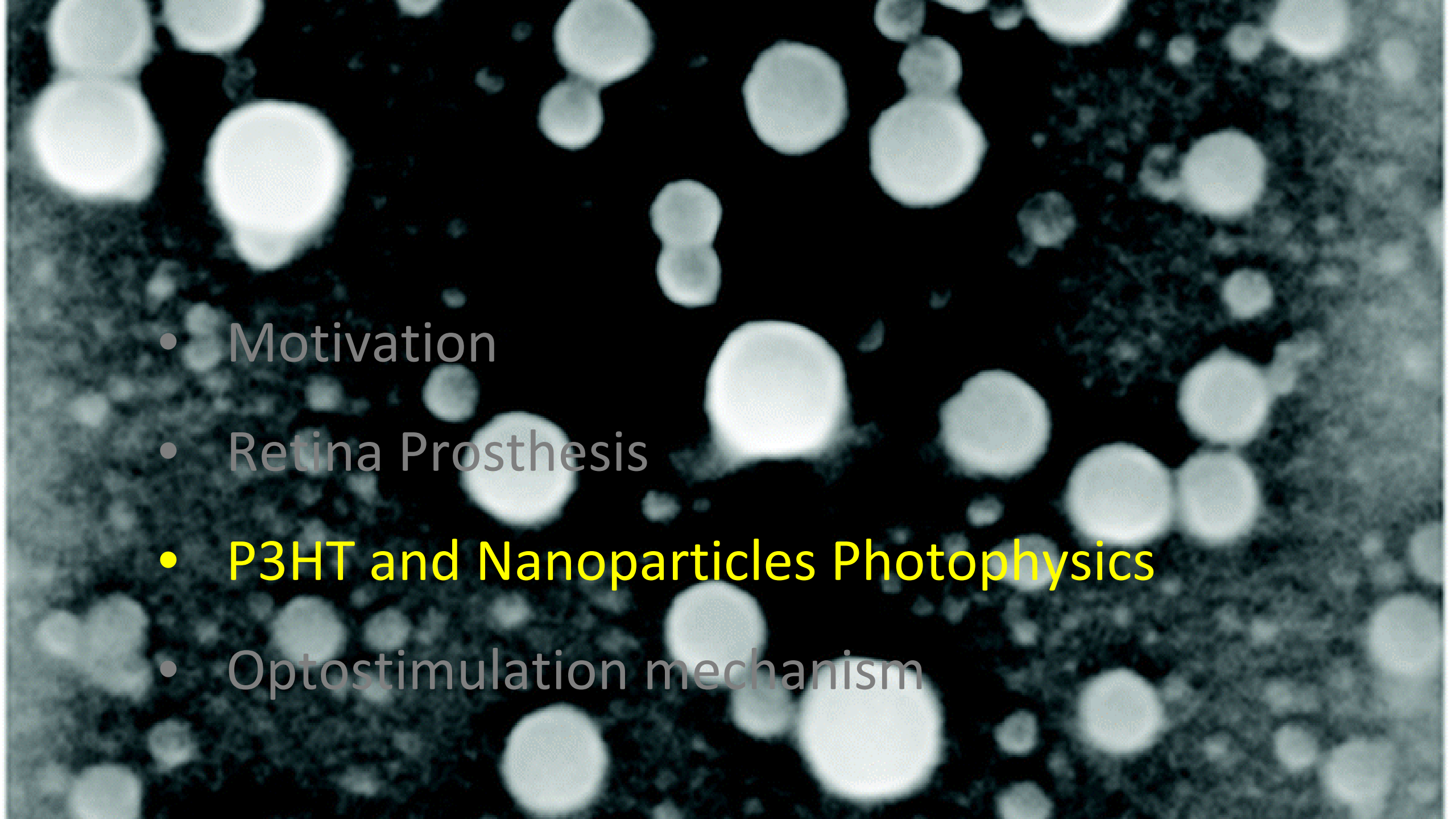
Visual Acuity



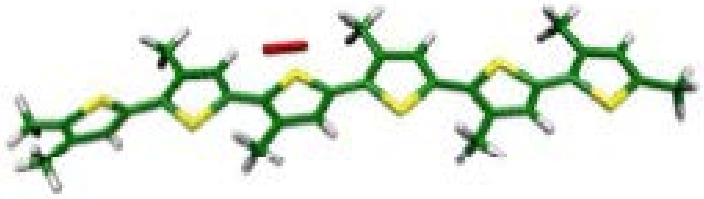




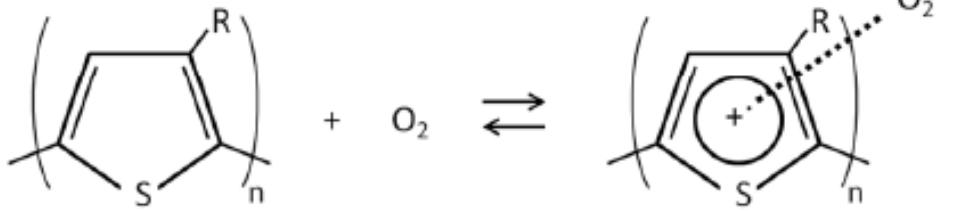



• Motivation
• Retina Prosthesis
• P3HT and Nanoparticles Photophysics
• Optostimulation mechanism

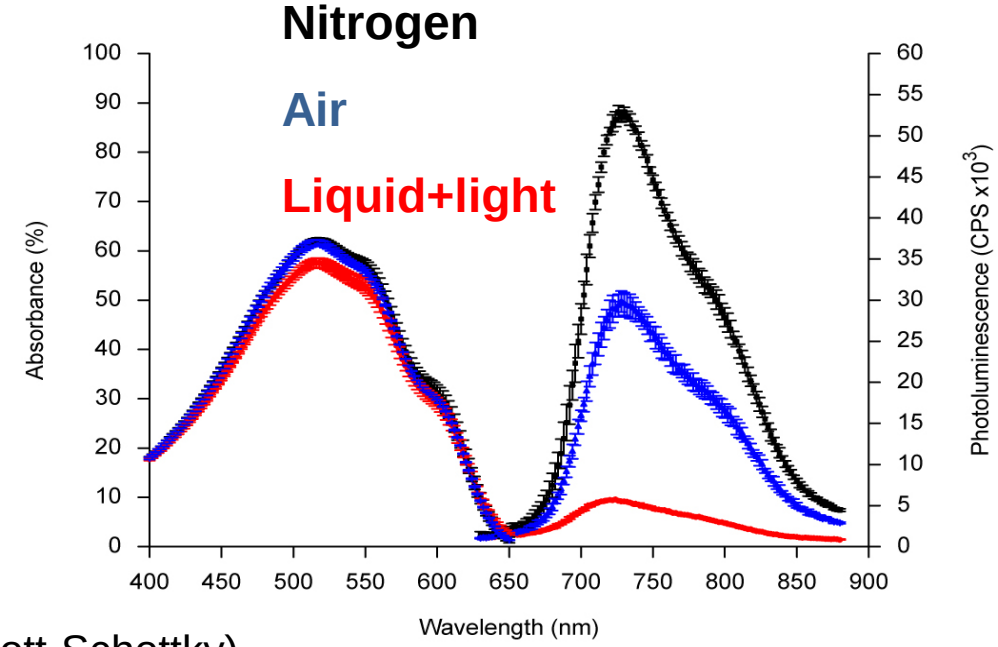
P3HT in contact with electrolyte



P3HT:$^3O_2$



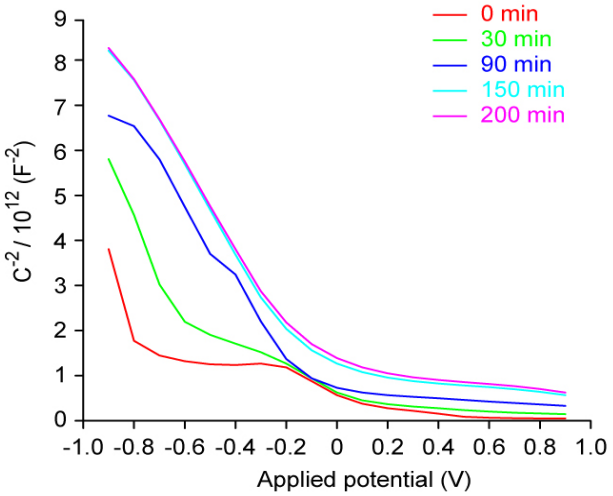
$P3HT + O_2 \rightarrow [P3HT^+ : {}^3O_2^-]$



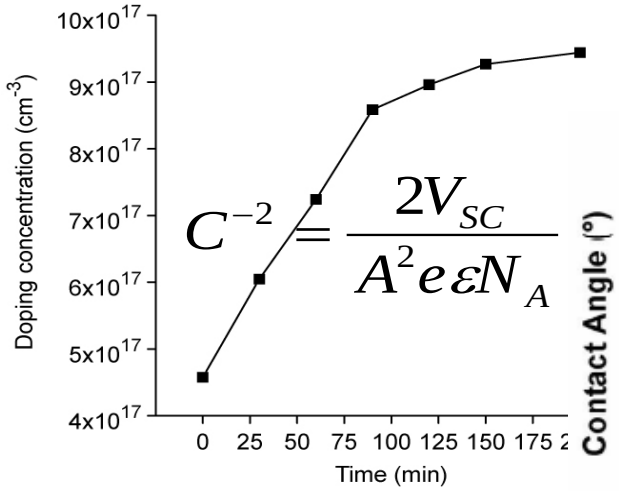
C_g = 17,8 nF

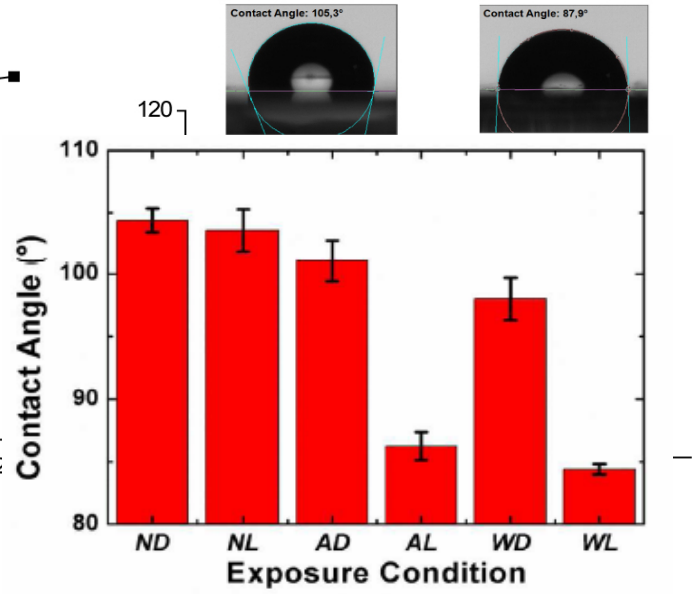
C_{exp}=180 nF

d < 15 nm



(Mott-Schottky)

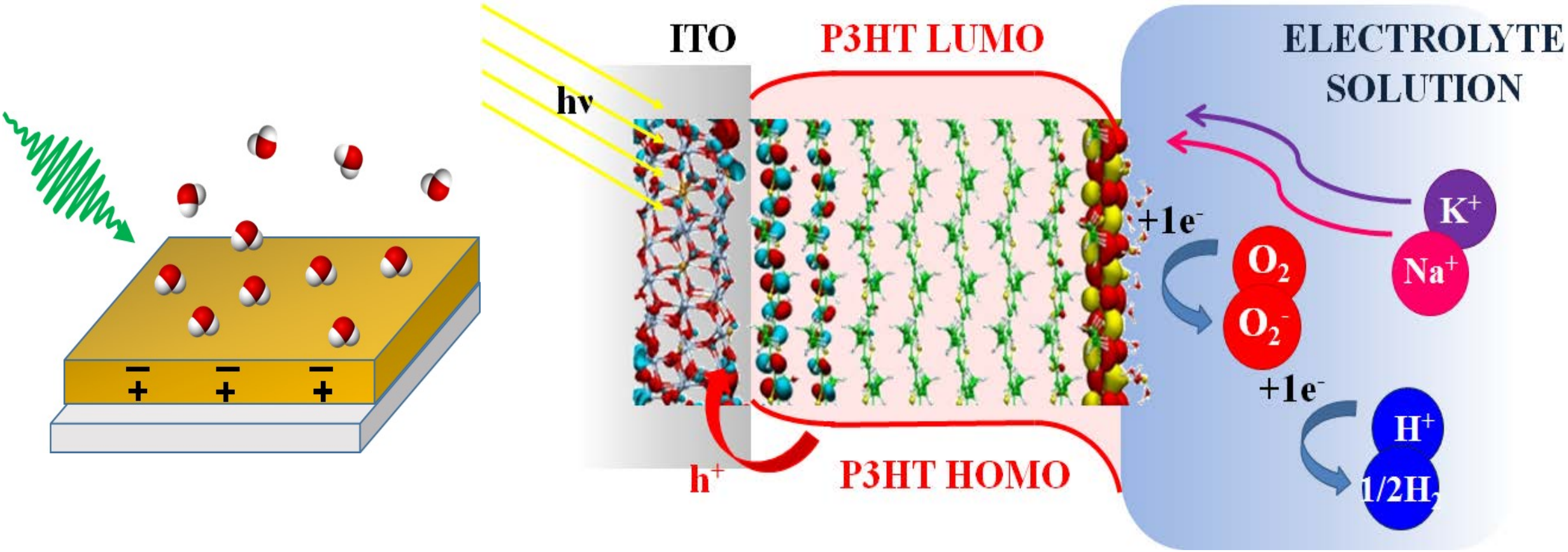




Nature Photonics 7, 400 (2013), J. Phys. Chem. C 118, 6291(2014)

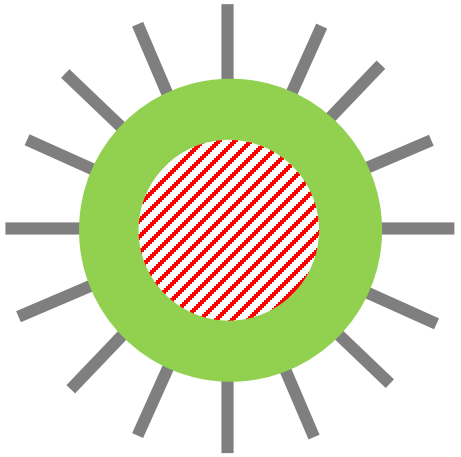
Surface Polarization Drives Photoinduced Charge Separation at the P3HT / Water Interface

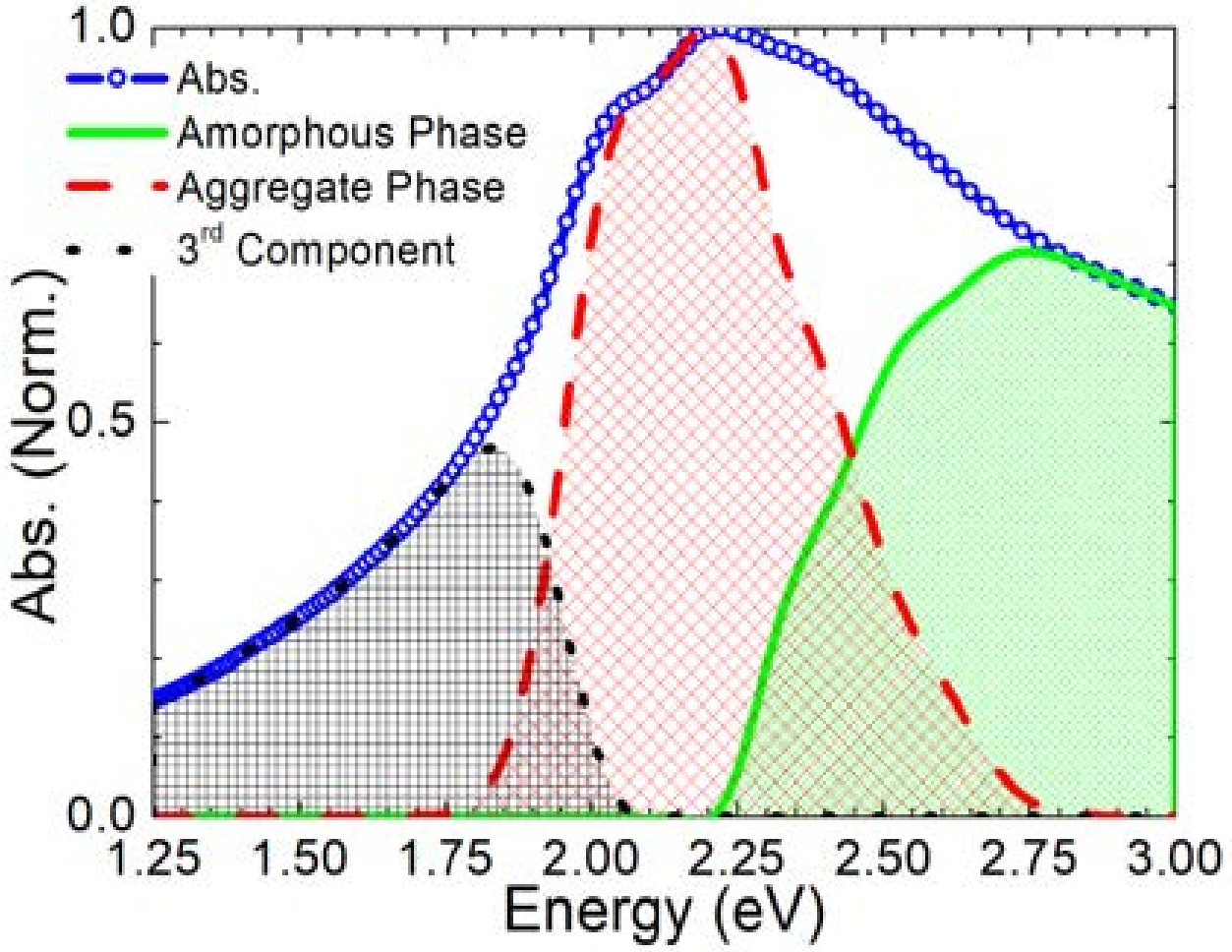
P. Salvatori, E. Mosconi, M. Saba, A. Mattoni, H. Li, J-L. Brédas, F. De Angelis



ACS Energy Lett. , 2016, 1 (2), pp 454–463

Nanoparticle Absorption





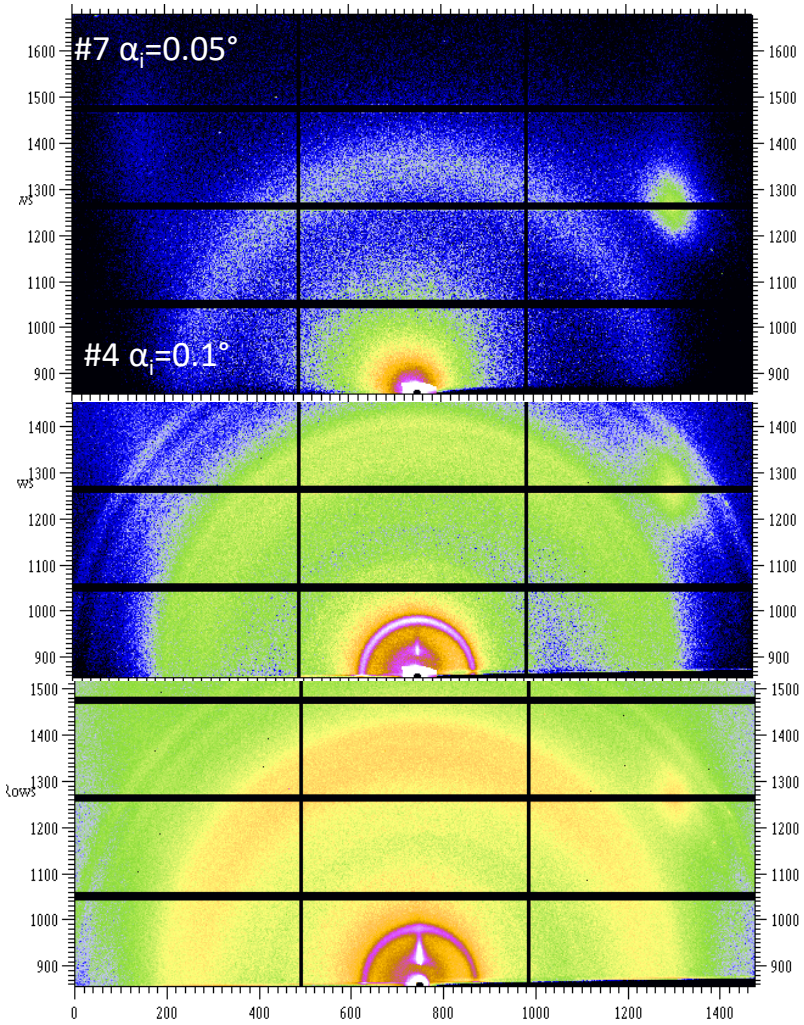
Aggregates ~24%

Exciton bandwidth W=33 meV

E. Zucchetti *et al.*, *J. Mater. Chem. B*, 2016.

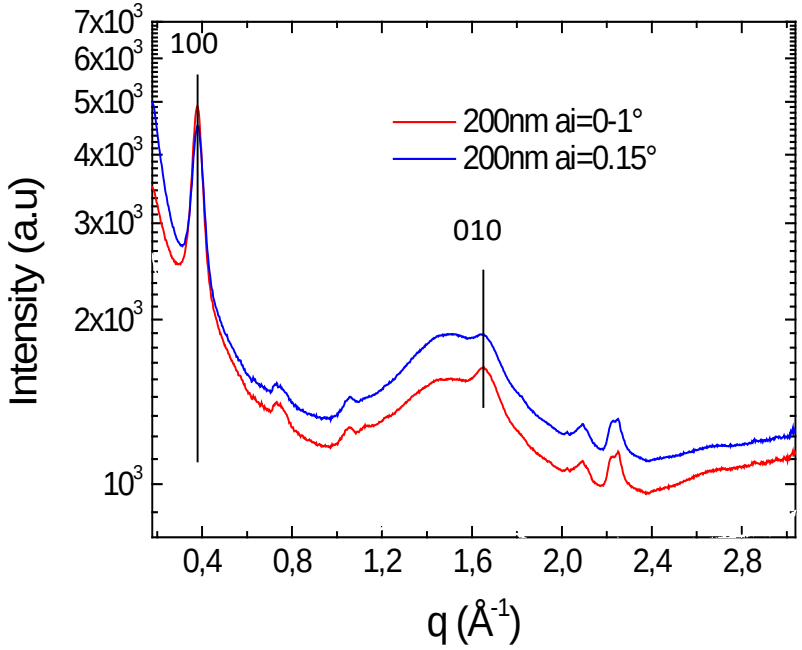
I. Bargigia et al. ChemBioChem 2018, 19, 1 – 6

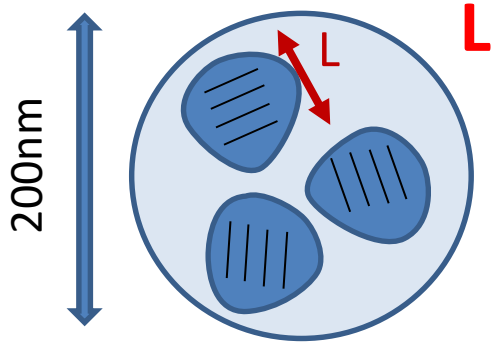
GIWAXS of P3HT NPs (200nm) spry coated on silicon



d_{100}=1.67nm → P3HT lamellar stacking

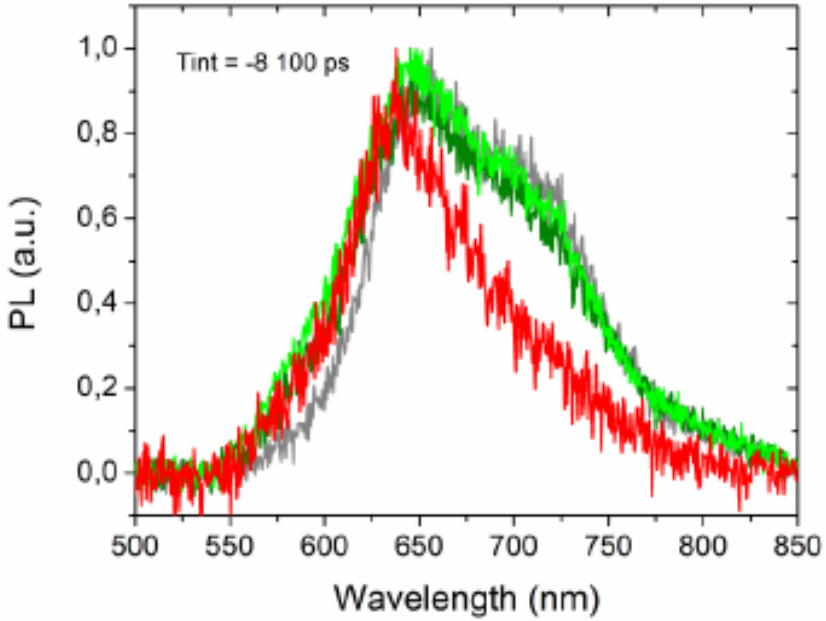
d_{010}=0.38nm → P3HT π-π stacking

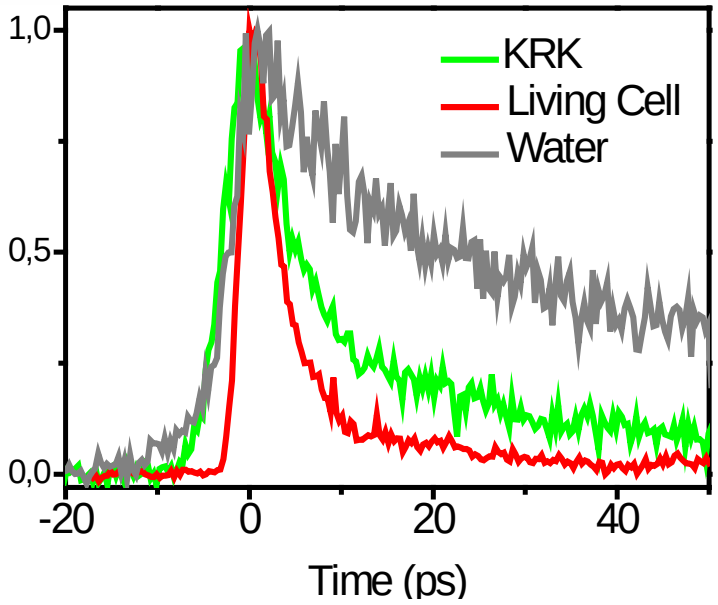




L ~ 12 nm

TRPL

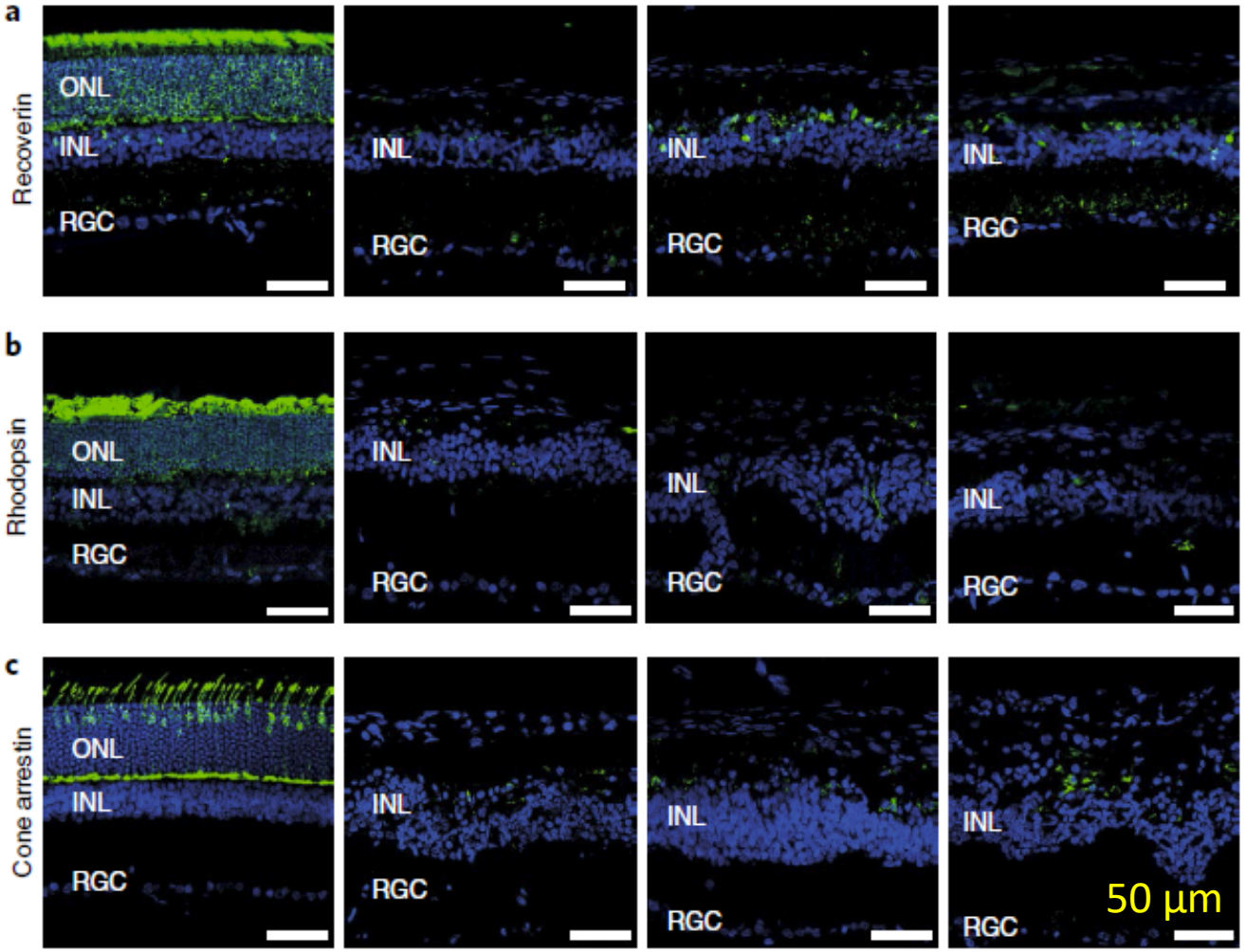


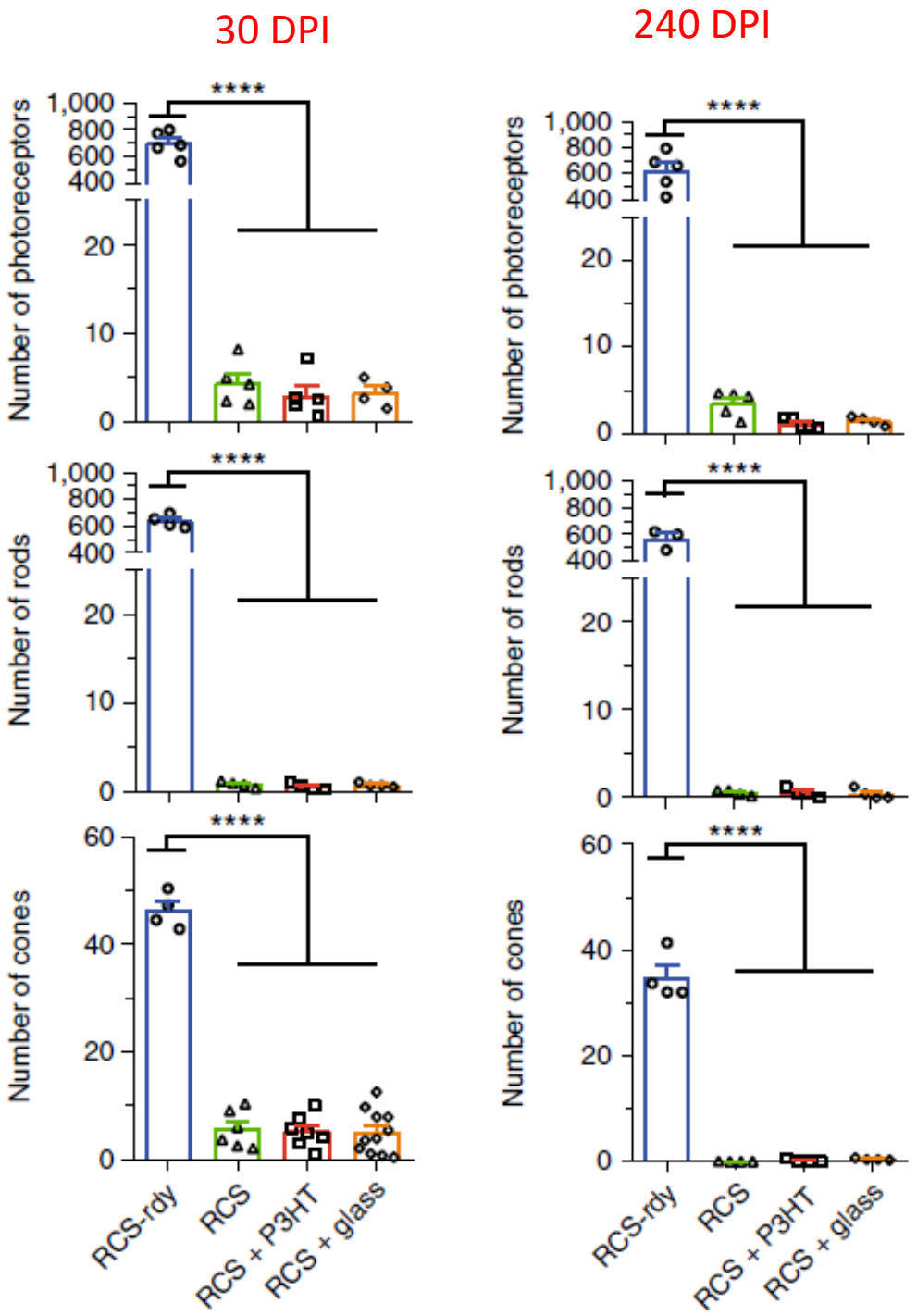


Fabiola Liscio CNR-IMM Bologna (I)

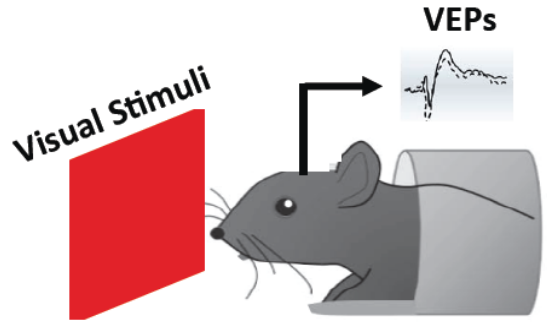
- Motivation
- Retina Prosthesis
- P3HT and Nanoparticles Photophysics
- **Optostimulation mechanism**

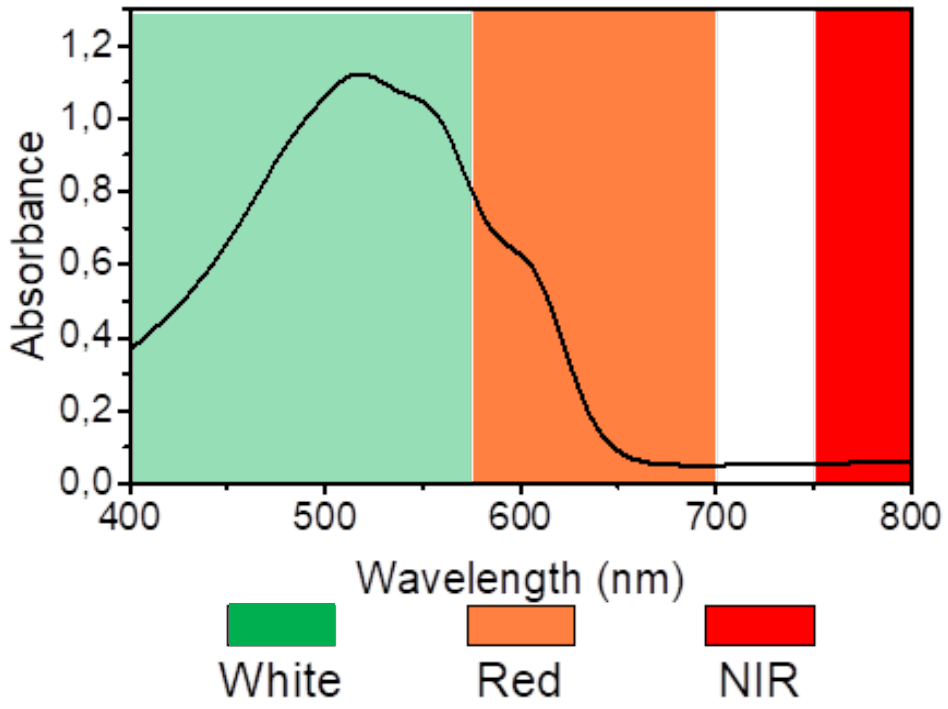
P3HT NPs do not promote photoreceptor survival in dystrophic retinas

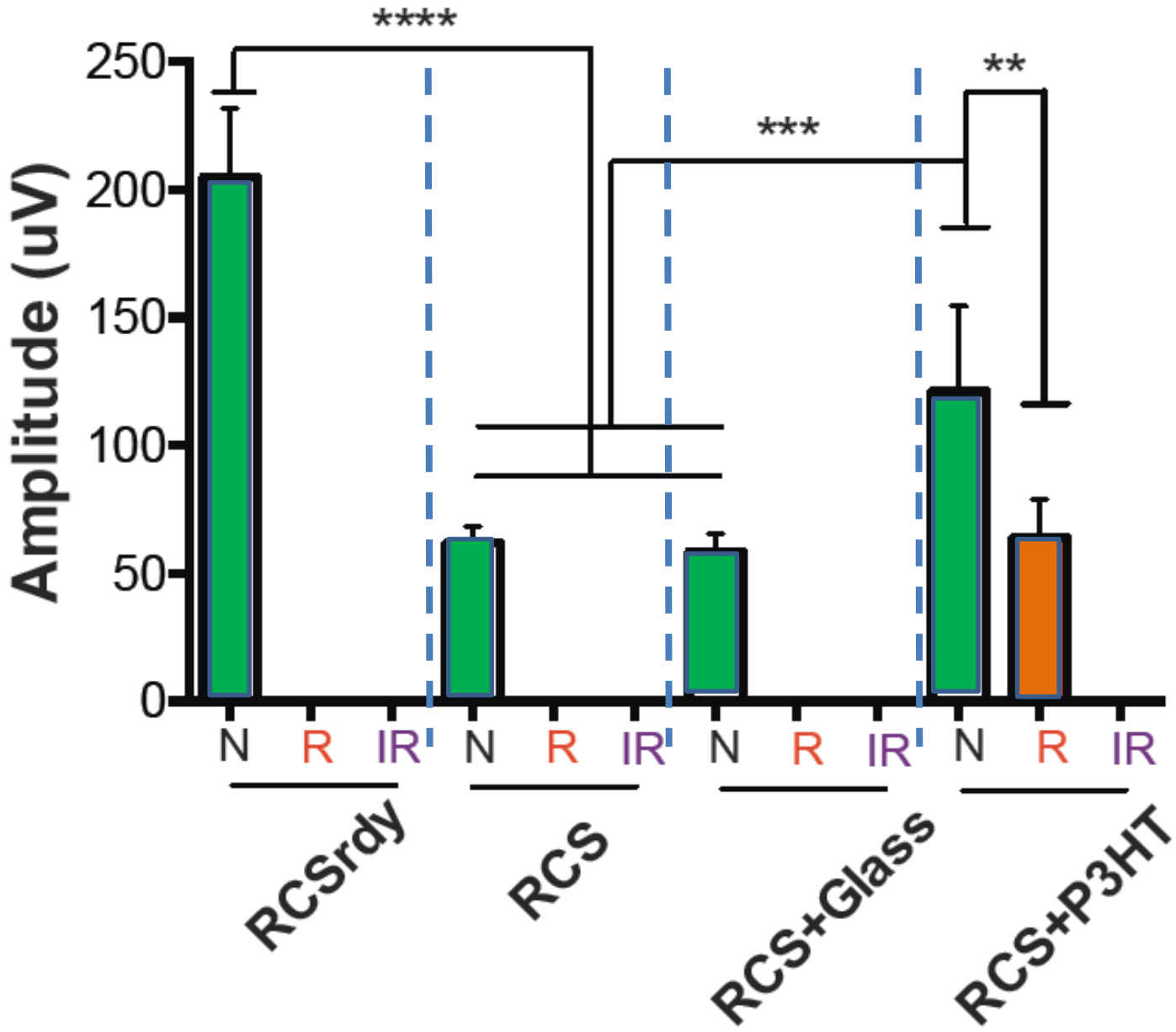




Experimentum crucis



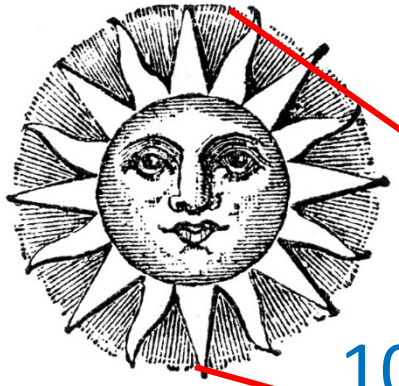




Nature Nanotechnology 15 (8), 698-708 (2020)

ILLUMINANCE [lux=lm/m^2]

Sun Light 10^4-10^5 lux
TV studio 10^3 lux
Office 500 lux
Moonlight 1 lux

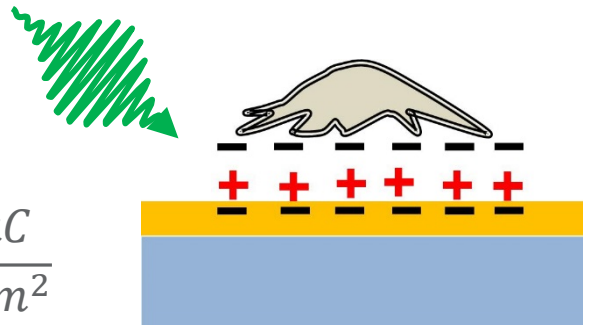


10 W/cm^2

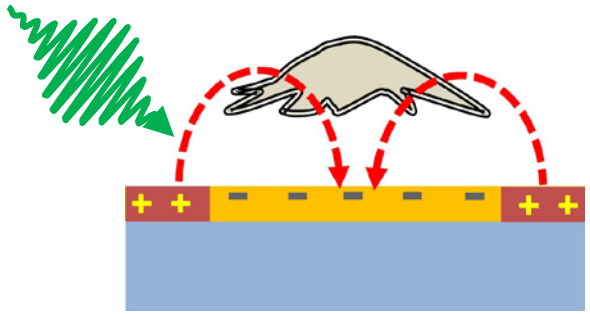
Office (500 Lux) ~ 25 mW/cm^2

Photo-excitation mechanisms

$Q_m = 10\ \frac{\mu C}{cm^2}$



CAPACITIVE

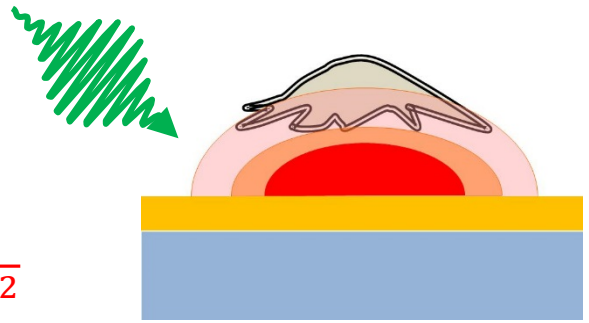


FARADAIC

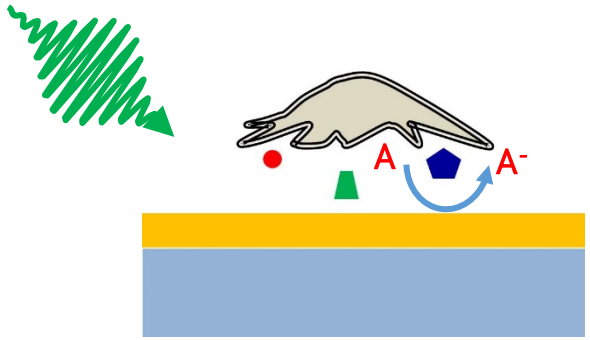
$i_m = 10\ \mu A$

$J_m = 1\ \frac{kA}{cm^2}$

$I = 1 \frac{W}{cm^2}$



THERMAL



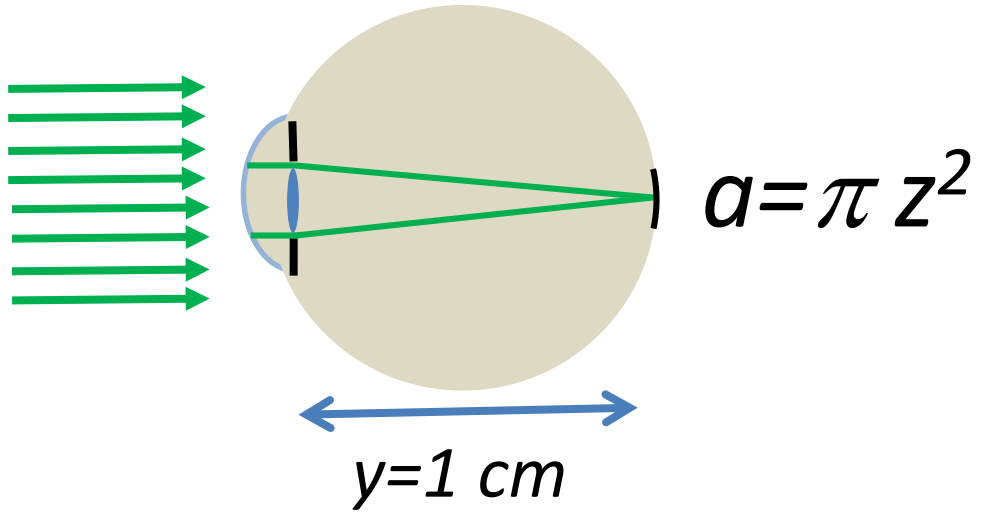
CHEMICAL

$Q_m = 1\ \frac{\mu C}{cm^2}$

Pupil reflex

I (corneal) = 20 lux= 20 lm/m²
λ=555 nm
2p=0.1 cm (pupil diameter)

$$P = I \times \pi p^2$$



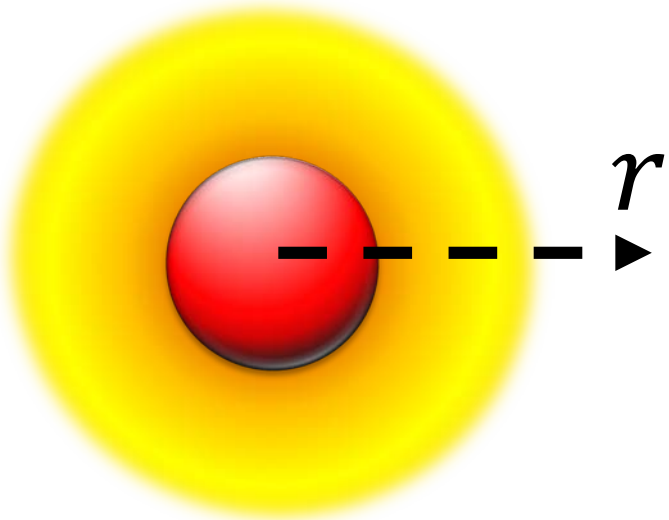
$$z = tg\vartheta \times \mathrm{y} \approx \vartheta \times \mathrm{y} \cong 1{,}22\frac{\lambda}{2p}\mathrm{y} = 7 \cdot 10^{-4}\ cm$$

$$I_R = \frac{P}{\pi z^2} = I\frac{p^2}{z^2} \approx 15\frac{mW}{cm^2} \ll 1\frac{W}{cm^2}$$

In VIVO thermal effect can be ruled out

Nanoparticle heating:

$$\Delta T = \frac{I_0 \pi R_{NP}^2}{4\pi k r}$$



I_0: light intensity (1 mW/cm^2)

R_{np}: Nanoparticle radius (175 nm)

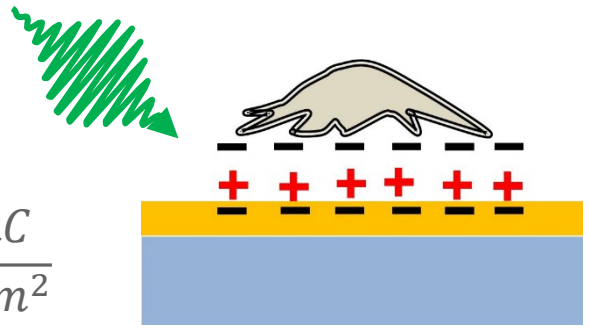
k: thermal conductivity of water (0.6 W/mK)

r: distance from nanoparticle centre

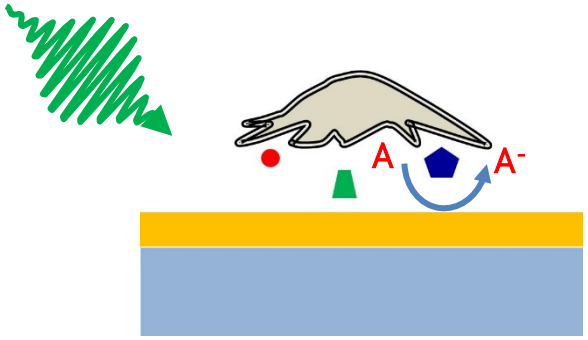
At the particle surface: $\Delta T \sim 10^{-7}$ K

Photo-excitation mechanisms

$Q_m = 10\ \frac{\mu C}{cm^2}$



CAPACITIVE



CHEMICAL

$Q_m = 1\ \frac{\mu C}{cm^2}$

ORGANIC NANOPARTICLES

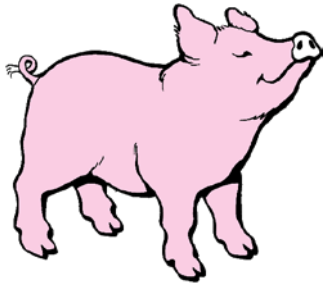
Transformational potential:
Novel approach for neuronal stimulation and for the cure of retina and brain diseases

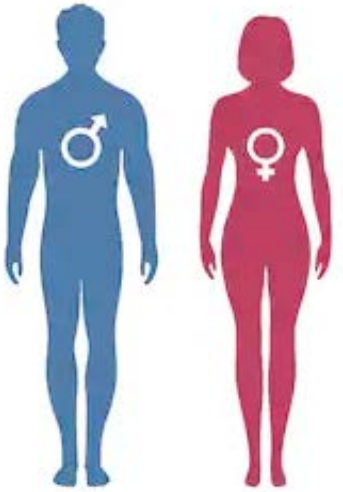
Cure degenerative blindness

Future perspectives in brain stimulation

Future Perspectives

Transferring to human experimentation





Funding

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