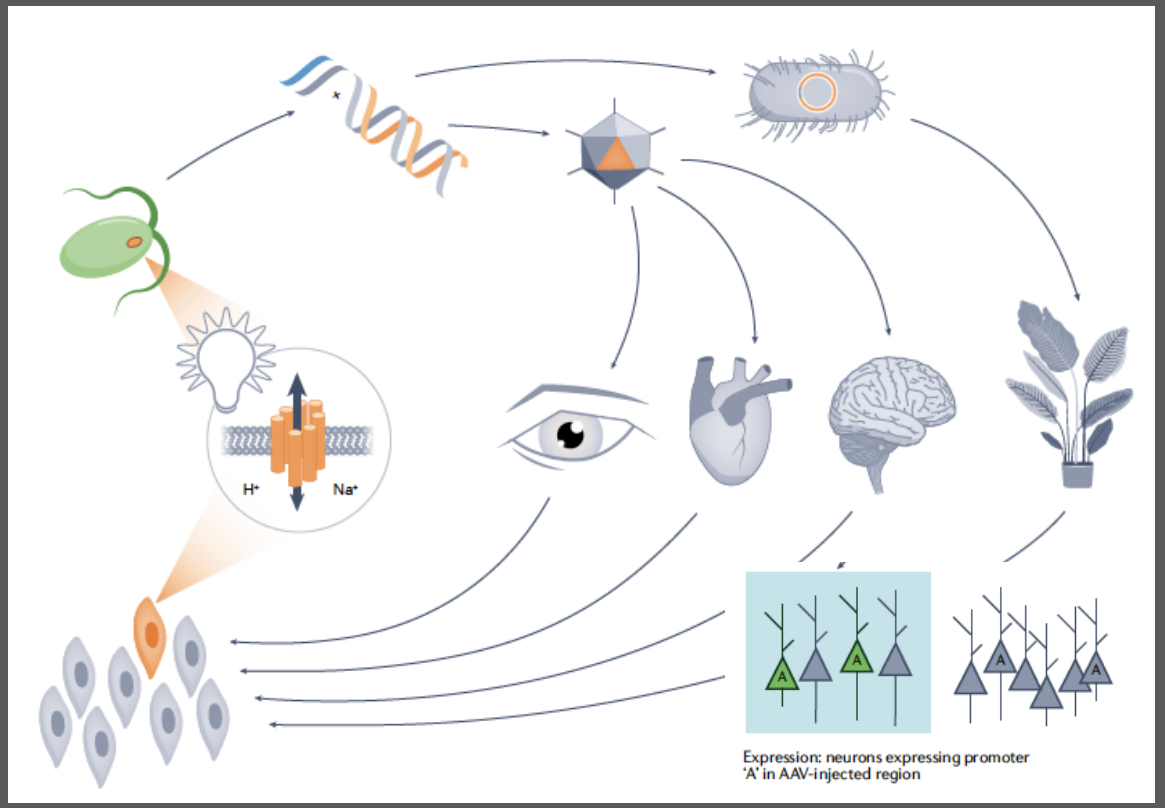
Novel sensory Photoreceptors and the Power of Femtosecond spectroscopy

Peter Hegemann

Humboldt-Universität zu Berlin

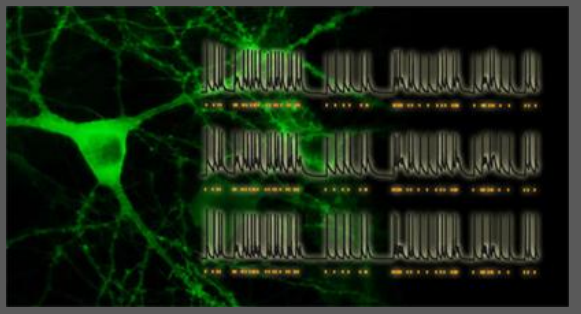
ELI Ultrafast Science Workshop
12.2.2026

Optogenetics,
a technology that makes cells light-sensitive



Emiliani et al. 2022 Nat. Rev. Meth. Prim.

Application of light sensitive ion channels

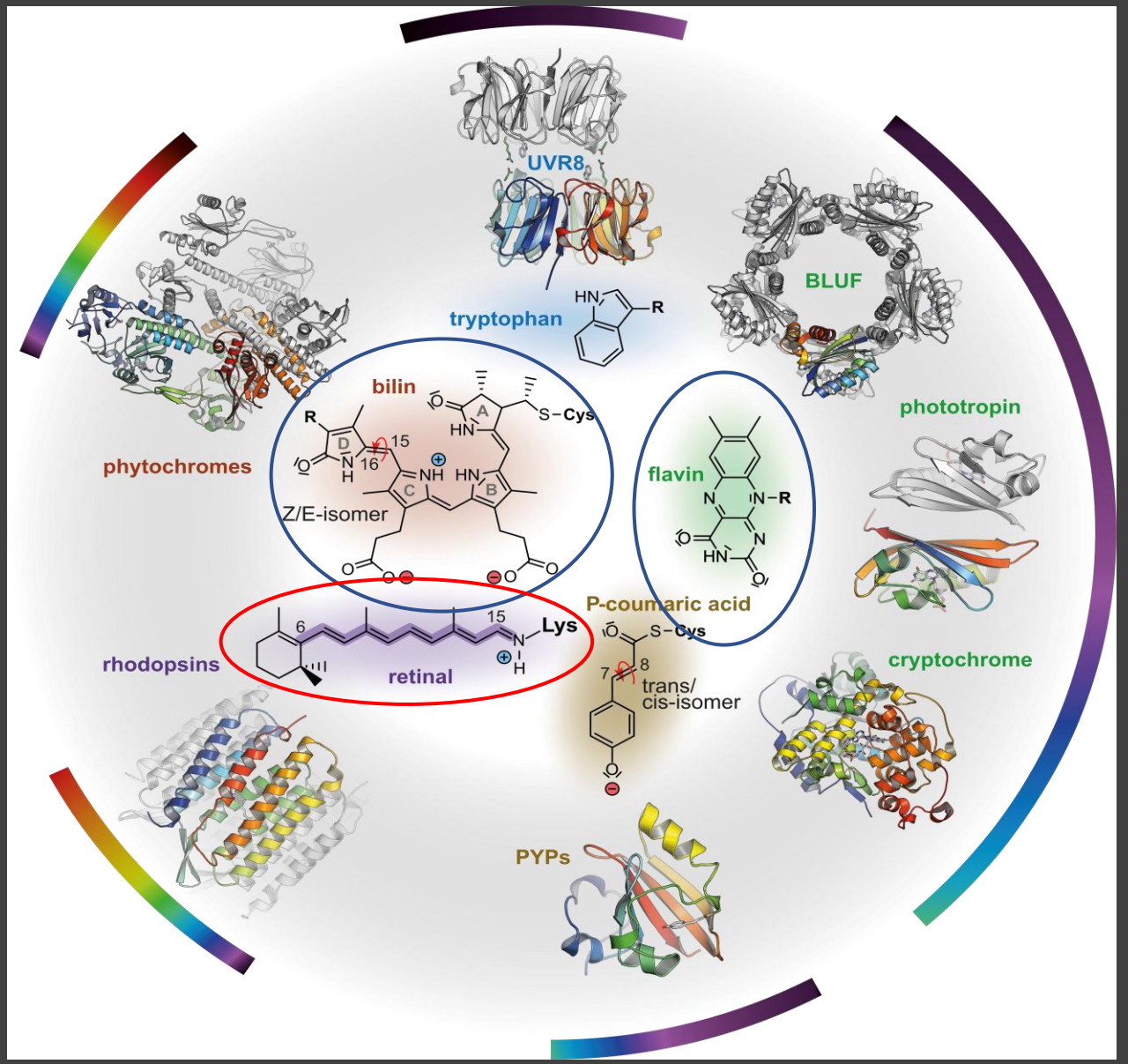


Boyden et al.2005 Net Neur.

New York Times

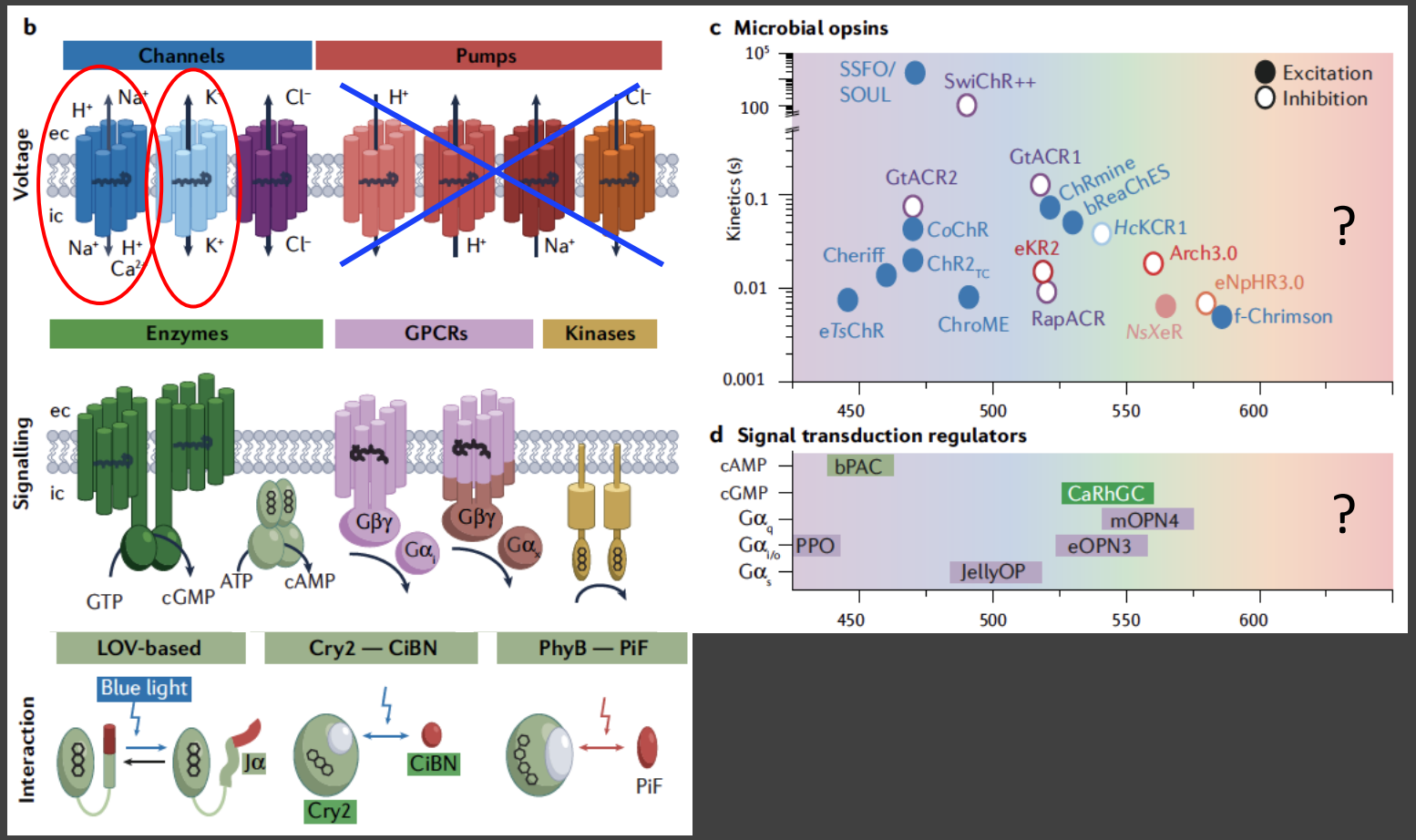
Sleep
Locomotion
feeding
Vision
Hearing
Sexuality
Autism
Addiction
Anxiety
Parkinson
etc.

Only a small number of natural chromophores



Enno Schiewers

„Application of light modulated channels, enzymes and GPCRs“

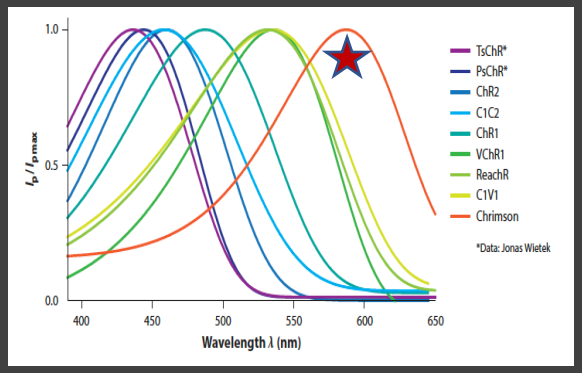


Retinal Therapy by Application of a red sensitive Channelrhodopsin

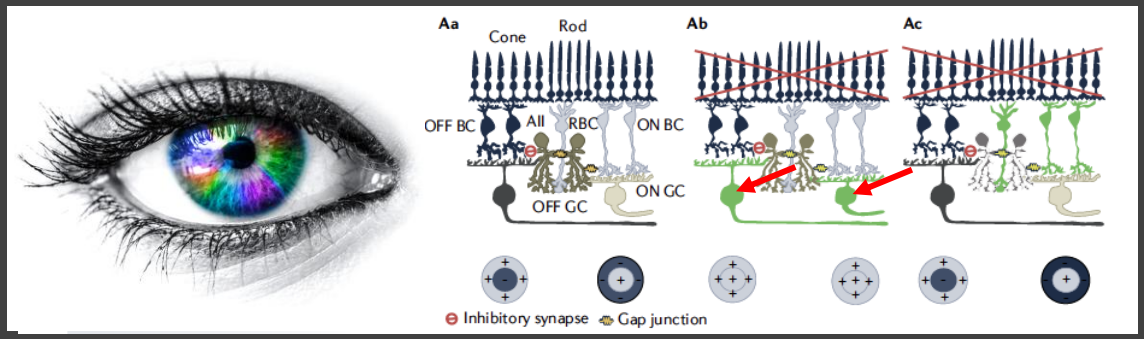
the 600 nm barrrier

Channelrhodopsins

Chrimson



The photoreceptors
for phototaxis in motile algae



Incorporation of
red-sensitive
Chrimson

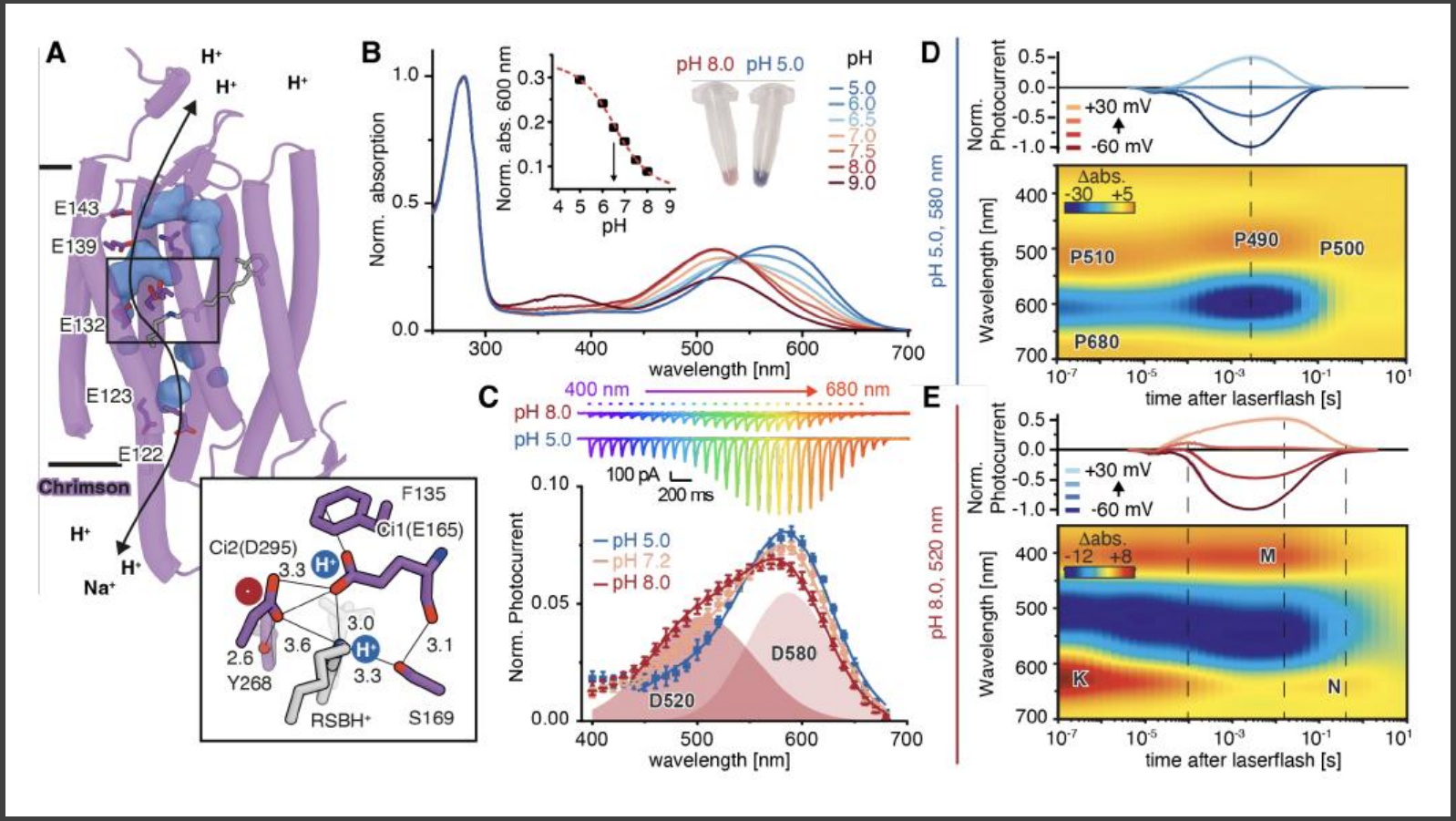
Jose
Sahel

Botond
Roska

Sahel et al. 2021 Nature Medicine

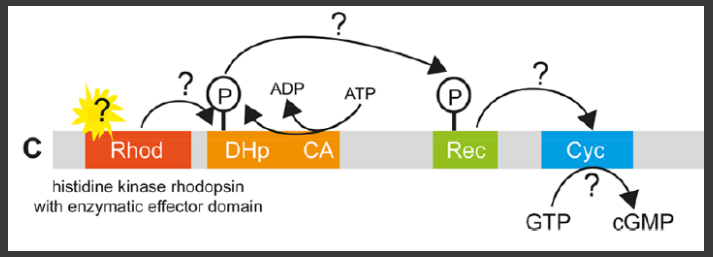
5

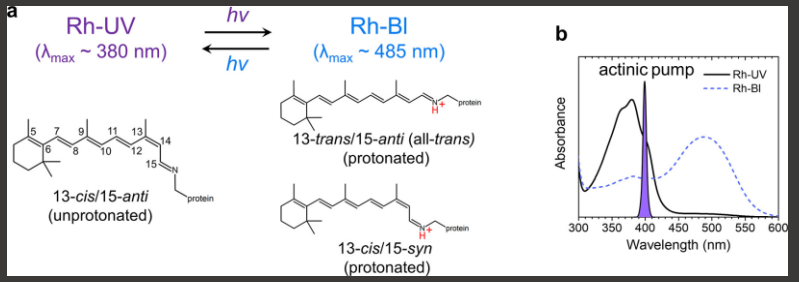
Chrimson is not ideal

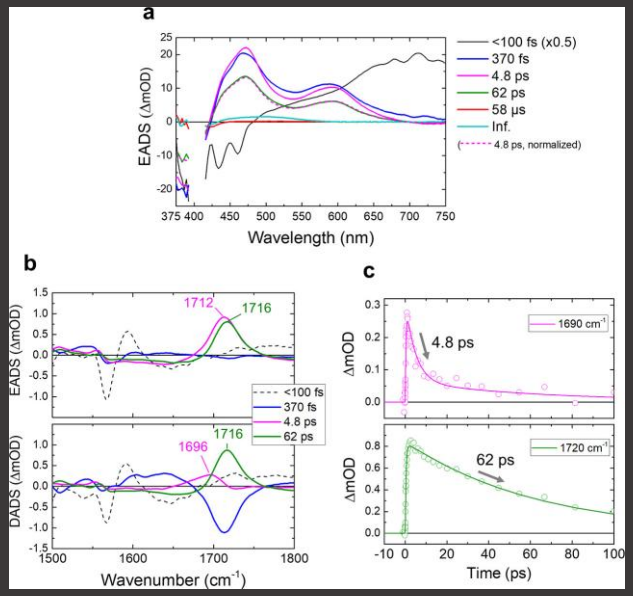


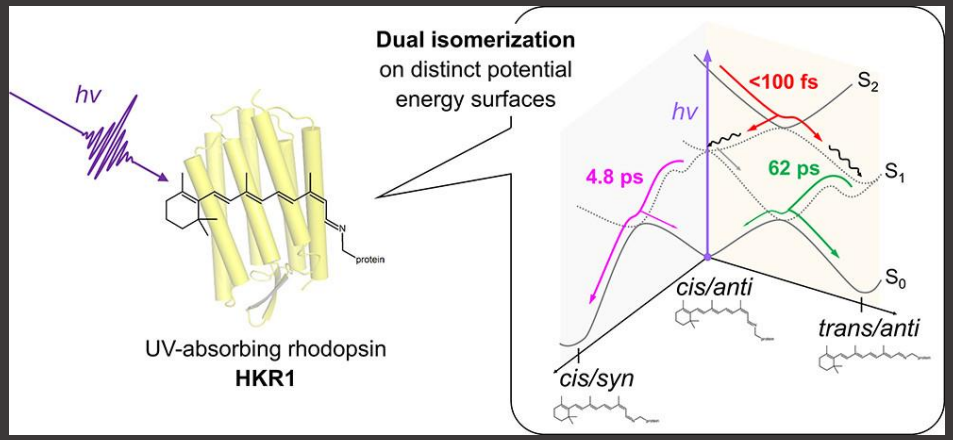
Chrimson conducts H^+ and is pH-dependent

Dual Photoisomerization in a UV-Absorbing Rhodopsin









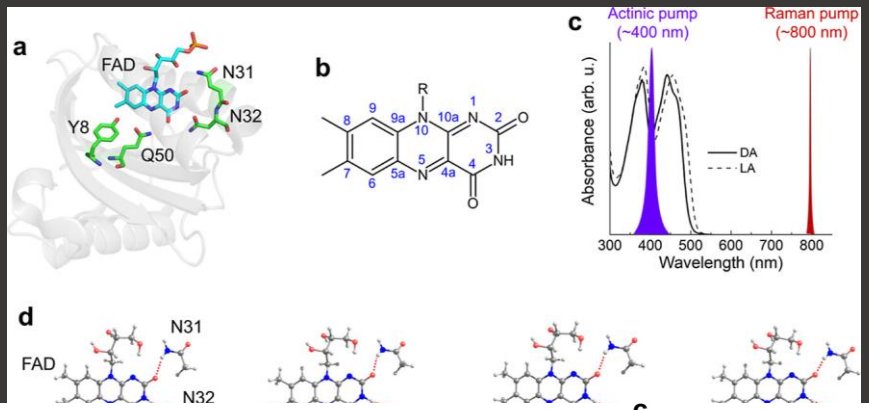
John Kennis
Amsterdam

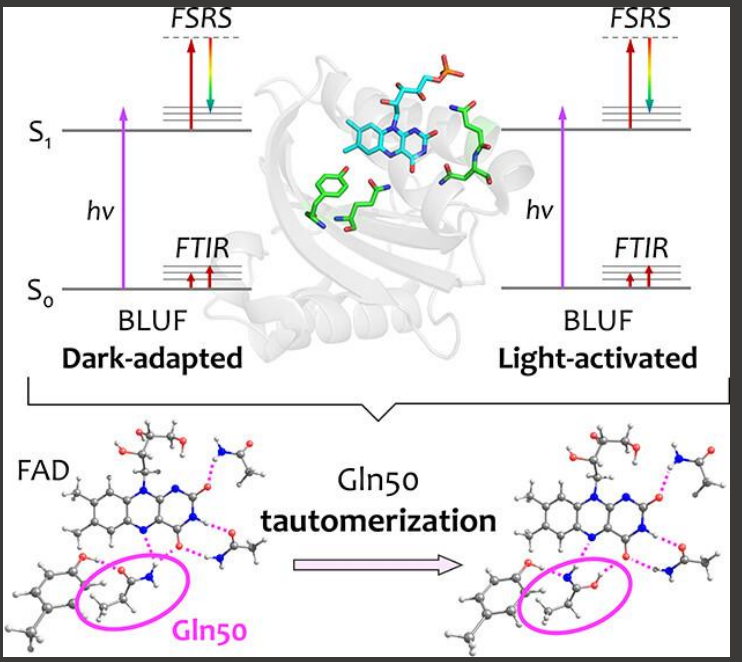
Miroslav Kloz
ELI Praque

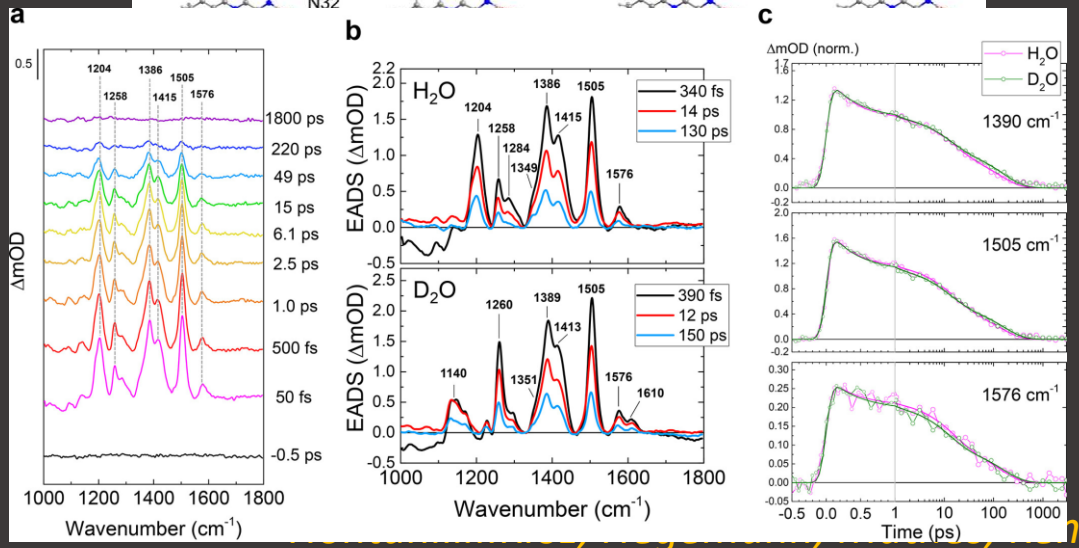
Hontani ….Kloz, Hegemann, Kennis 2020 J. Am. Chem. Soc.

VU Amsterdam
ELI Praque

Solving a long standing question about the mechanism of Blue Light Receptors Using Flavin (BLUFs)







Nonnis 2023 JACS

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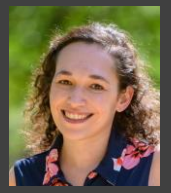
Bestrhodopsin from marine Algae

Phaeocystis antarctica

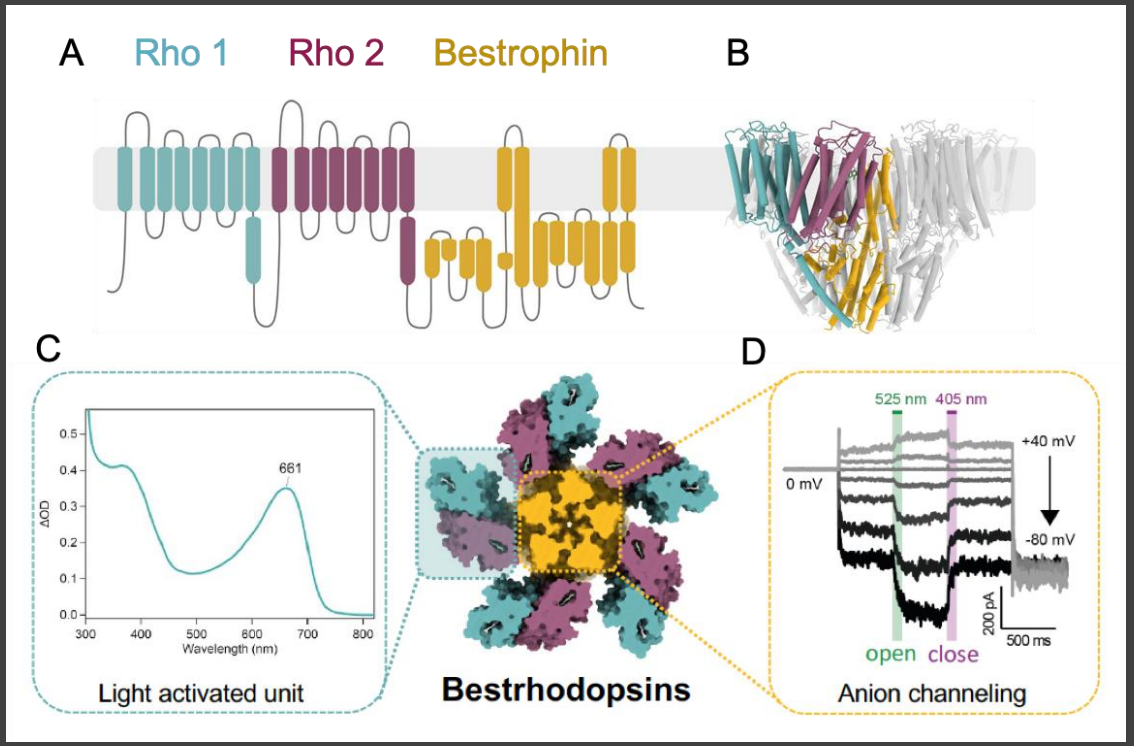
Oded Beja



Moran Shalev-Benami

Andrey Rozenberg

Johannes Vierock now Charité

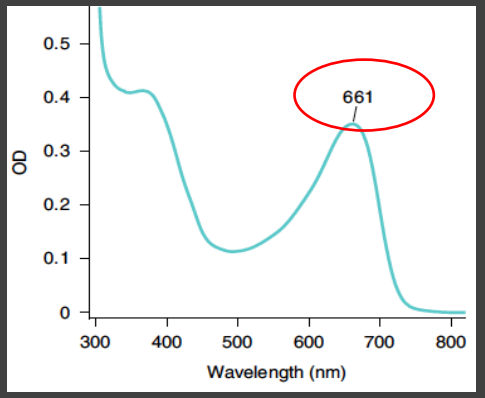


Karlodinium veneficum

large channels in algal chloroplasts

Rozenberg et al. 2022 *Nature Structural Biology*

Mysterious photoreactions of Bestrhodopsin
Bifurcation and reassembly



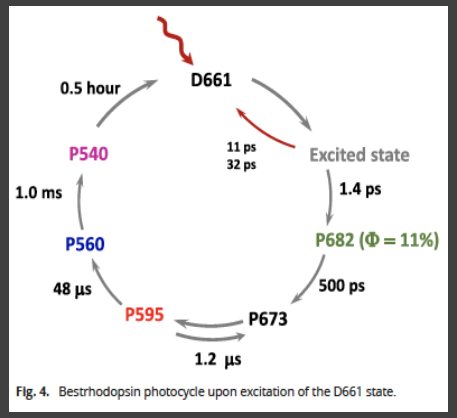
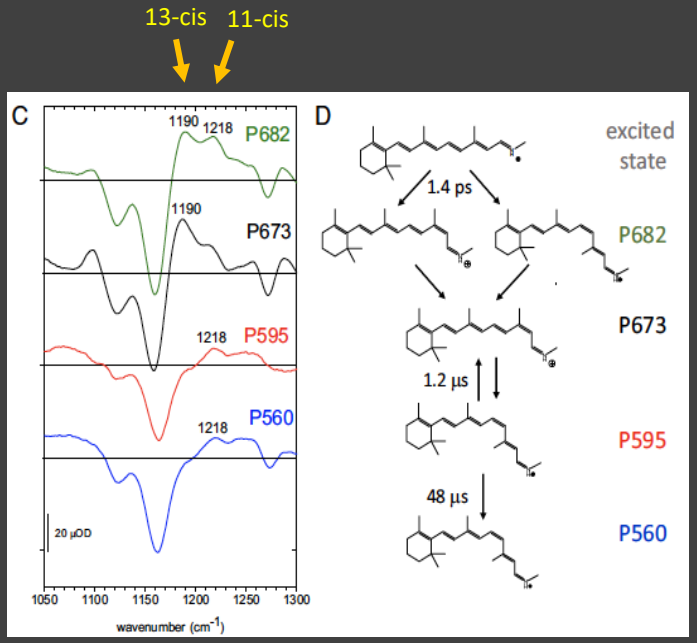


Fig. 4. Bestrhodopsin photocycle upon excitation of the D661 state.



all-trans

13-cis & 11-cis

13-cis

11-cis

11-cis

femtosecond-Raman

John Kennis
Amsterdam

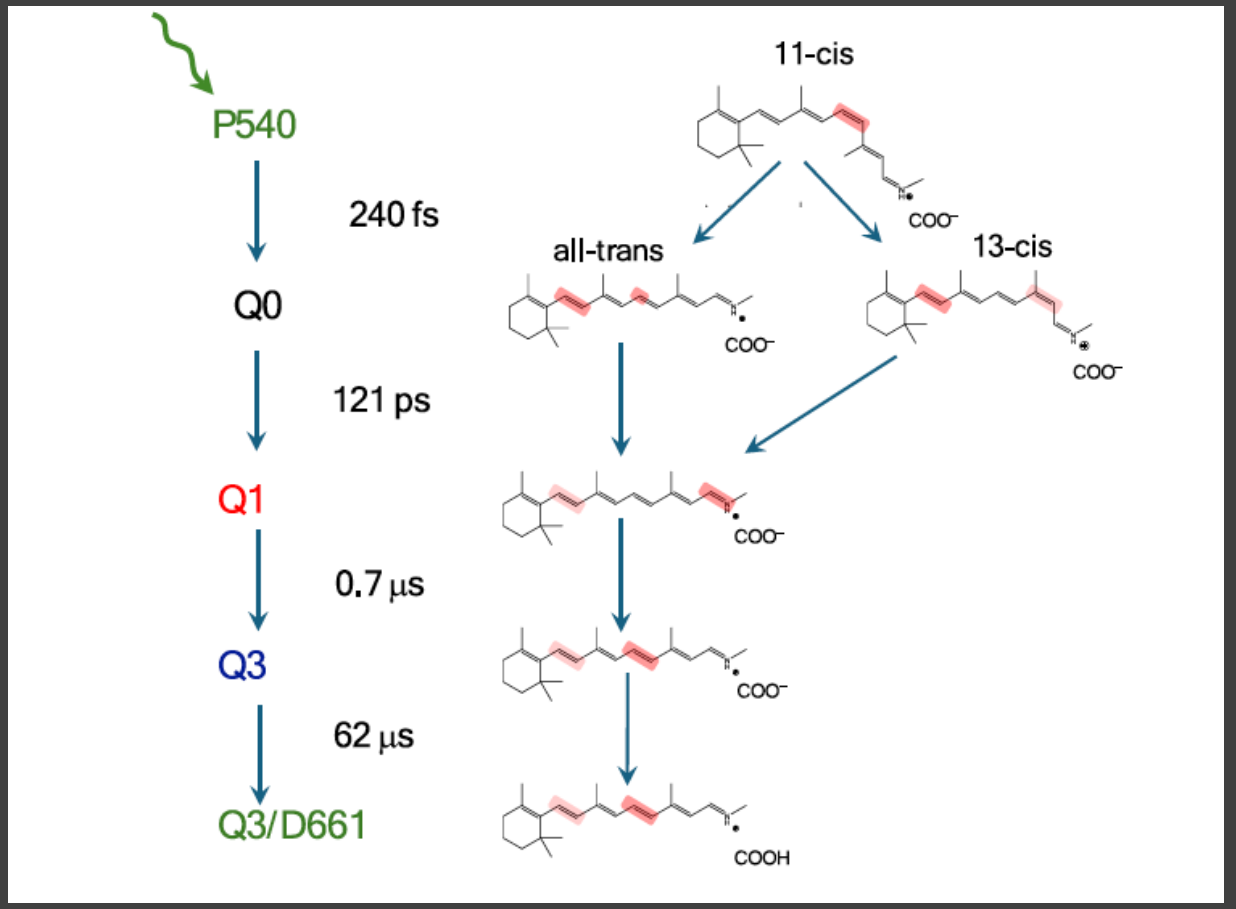
Miroslav Kloz
ELI Praque

all-trans → 13-cis/11-cis → 13-cis → 11-cis → all-trans
as studied by fs-UV-Vis and fs Raman spectroscopy

ELI Prague
HU Berlin
VU Amsterdam

Kaziannis …….Kloz, Hegemann, Kennis 2024 PNAS

Backreaction, again with Bifurcation and Reassambly



During the forward and backward reaction 13-cis Retinal accurs as an intermediate

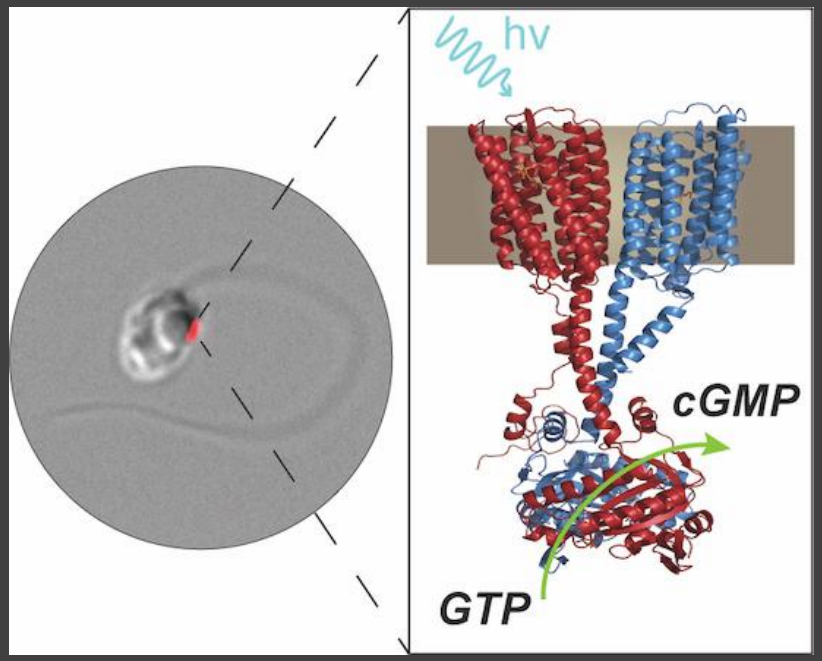
Bond distortions in red

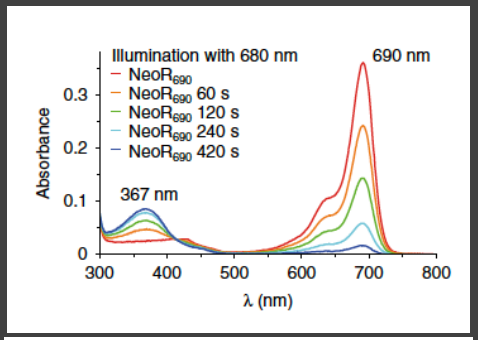
Broser…..Hegemann, Kloz, Kennis 2025 JACS

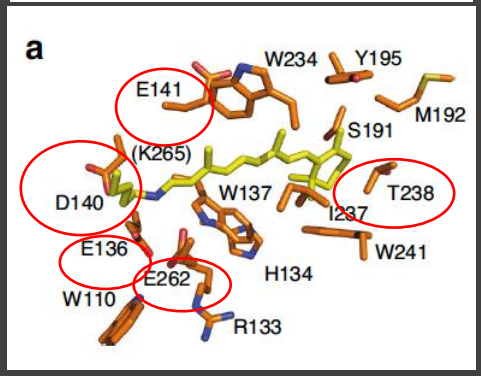
HU Berlin
VU Amsterdam
ELI Prague

NeoR, far-red **sensitive and most bizarre** Rhodopsin from *Rizoclosmatium globosum*

Matthias Broser



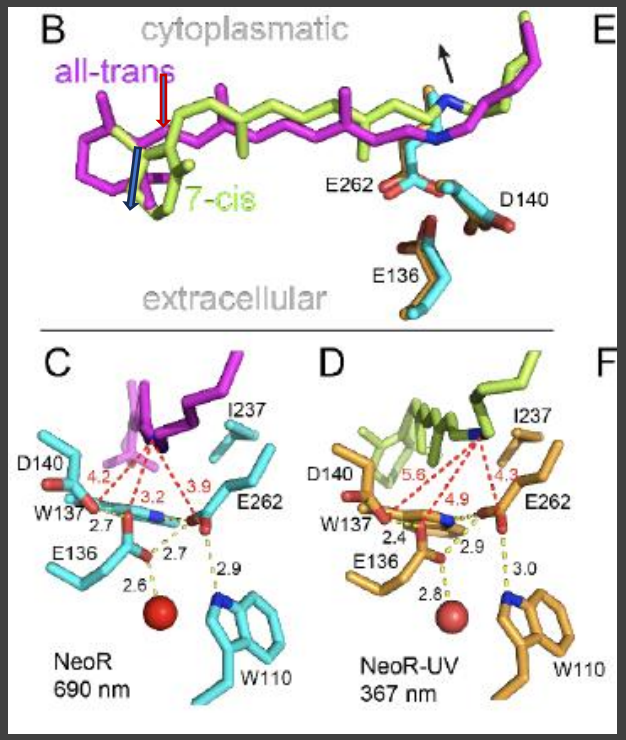


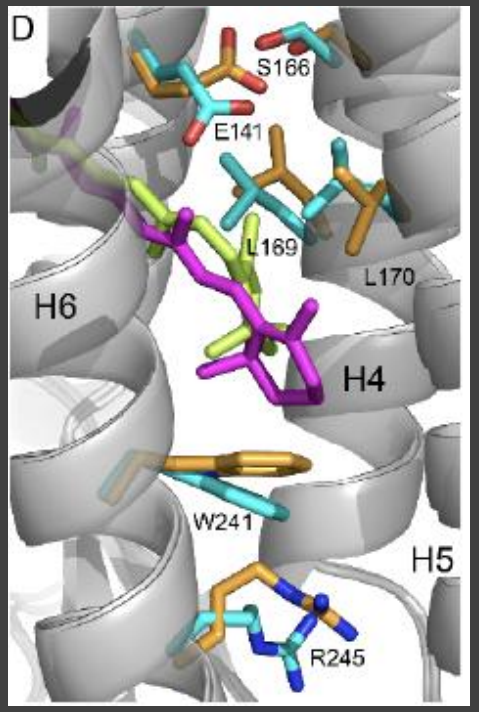


Far-red absorption
high fluoresence

Broser et al. 2020 Nature Comm, Busse et al. 2025 EMBO J.

A real structure of NeoR





Kirill Kovalev
EMBL Hamburg

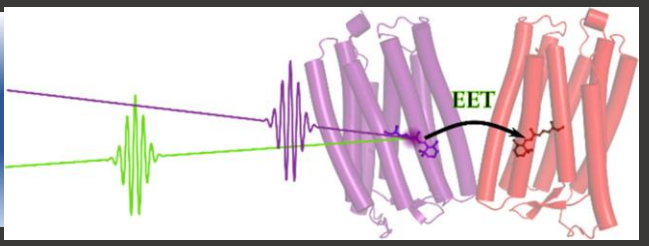
Matthias Broser

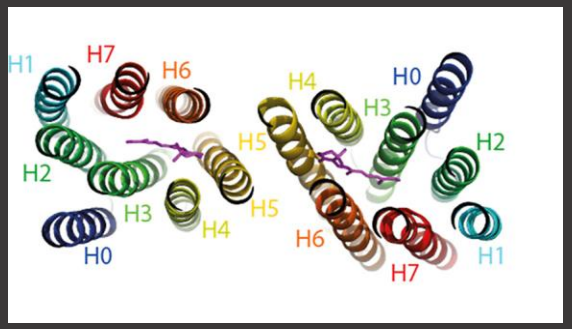
The new structure shows a Retinal Schiff Base without hydrogen bridges which is the secret for NIR absorption and a modified ring structure for NeoR-UV, which causes deprotonation of the chromophore

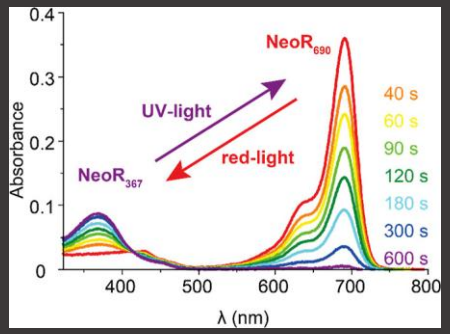
Kovalev et al. unpublished

HU-Berlin & EMBL Hamburg

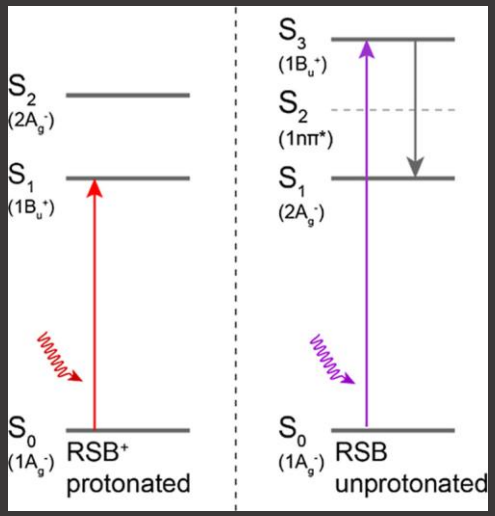
Rh-Rh Energy transfer

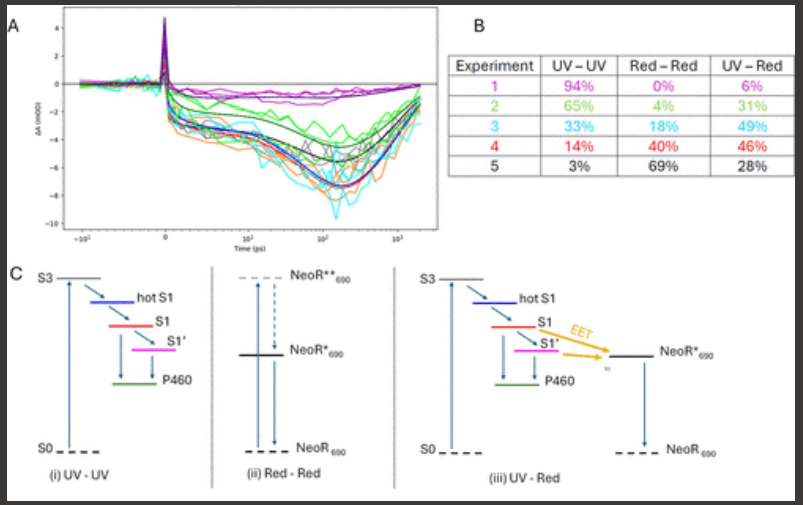






First discovery of such an energy transfer





VU Amsterdam
HU Berlin
ELI *Dolní Břežany,*

Van Stokkum, …..Hegemann, Kloz, Broser, Kennis 2025 JACS

Summary: UV to Far-red light sensing.

- To understand photoreceptor function we need:
  - Physiological characterization
    - Highly purified protein
  - Spectroscopy on times scales ranging from femtoseconds to seconds
    - High resolution structures
    - Time resolved crystallography

We finalized 23 publications with the ultrafast spectroscopist John Kennis (VU Amsterdam)
6 publications with the fs Raman Expert Miroslav Kloz (ELI)

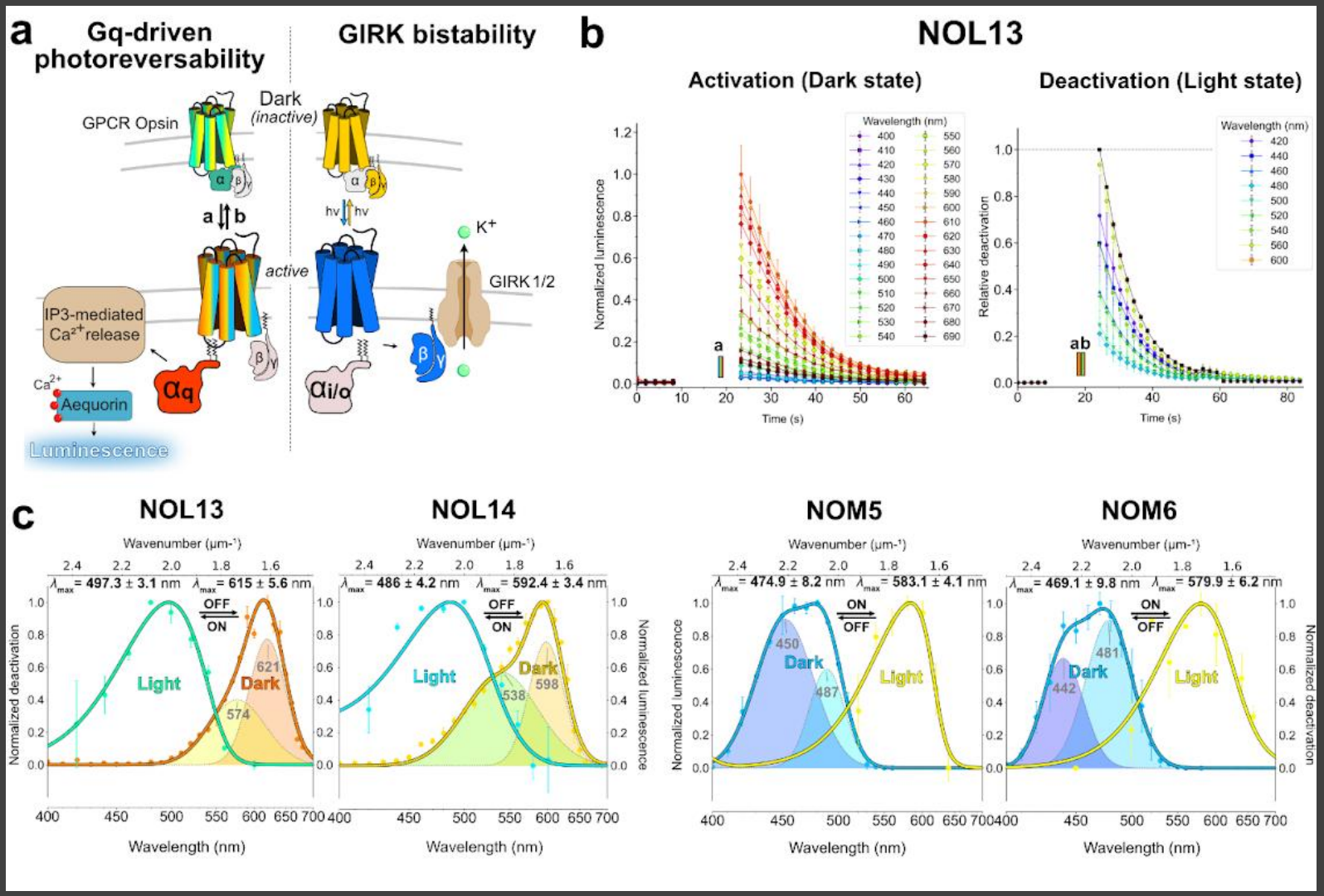
Acknowledgements

Hegemann Group 2023 during an excursion to Prag

Current Collaborators

- **John Kennis** / FU Amsterdam: fs spectroscopy
- **Miroslav Kloz** / ELI Prag: fs Raman
- **Igor Schapiro /** Dortmund Theory
- **Franziska Schneider-Warme** / Fr Cardiac optogenetics
- **Kirill Kovalev** / Hamburg: X-ray Crystallography
- **Marjorie Lienard /** Liege: Shrimp Rhodopsine
- **Megan Porter** / Hawai Shrimp Rhodopine
- **Oded Beja** / Haifa: functional genomics
- **Moran Shalev-Morani** / Weizmann: Cryo-EM

Action spectroscopy



Bistable rhodopsins with reversible switching